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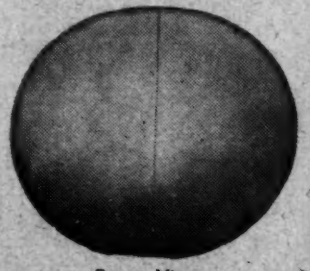
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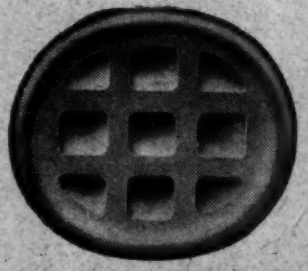
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BRITISH MEDICAL JOURNAL

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THE INDICATIONS FOR RADIO-IODINE TREATMENT OF THYROID CARCINOMA

BY

E. E. POCHIN, M.D., F.R.C.P.
N. B. MYANT, D.M.
GWEN HILTON, M.B., B.S., F.F.R.
A. J. HONOUR

AND

B. D. CORBETT, B.A.

(From the Department of Clinical Research, University College Hospital Medical School, London)

Bases of Selection

Certain thyroid carcinomata resemble normal thyroid tissue in having the capacity to concentrate iodine. Since radioactive iodine is chemically indistinguishable from normal iodine, such tumours will selectively concentrate radio-iodine. They may therefore be selectively irradiated by the intense local beta radiation which is emitted from radio-iodine. If the local concentration and retention of radio-iodine in the tumour is high enough relative to that in other body tissues, the local radiation within the tumour may be great enough to cause its destruction, without causing fatal or toxic effects in the body as a whole. In principle, therefore, the selection of cases for such treatment is simple. Complete surgical excision remains, of course, the treatment of choice if ever it is possible (Dobyns, 1951); otherwise, radio-iodine should be used to treat any thyroid carcinoma which can be shown, or can be induced, to take up radio-iodine sufficiently.

In practice, this criterion is complicated by several considerations. First, the detection of radio-iodine uptake, and the judgment of its adequacy, may be difficult, particularly if the tumour is adjacent to normal thyroid tissue and if repeated biopsies cannot conveniently be made. Secondly, uptake may be demonstrable after total thyroidectomy in a tumour in which no uptake could be detected before the thyroid was removed. It may therefore be necessary to select for thyroid ablation* those cases in which uptake cannot be shown but is likely to be demonstrable after thyroidectomy. This decision will be based on such indirect evidence as the histological differentiation of the tumour and perhaps its rate of growth. In such cases tests for uptake are repeated after thyroid ablation, and radio-iodine treatment is started if adequate retention can be demonstrated.

The most direct evidence of radio-iodine uptake in a tumour is obtained by examination of biopsy material, using methods which are discussed later. These biopsy methods, however, are often inadequate for the selection of cases for radio-iodine therapy, since repeated tests may be required for the uptake in one or in various metastases, and following thyroidectomy or other procedures designed to reveal or stimulate uptake, or during the course of treatment. Since frequent biopsies of carcinomatous tissue are rarely desirable, and even single biopsies of some metastases—for example, in lung or bone—may be impracticable, the study of radio-iodine uptake will commonly depend on methods of external counting, by which the localization of radio-iodine is detected with a counter external to the body.

In the following account the detection of radio-iodine uptake in thyroid tumours by biopsy and by external counting is illustrated; and the criteria used in selecting cases for thyroid ablation and for radio-iodine treatment are then discussed.

Radioactivity of Biopsy Material

If a test dose of radio-iodine is given, and tumour tissue is removed several days later, the selective concentration of radio-iodine by the tumour may be inferred by comparing the radioactivity per gramme of its tissue with that per gramme of, say, plasma removed at the same time. The radioactivities are readily compared by placing the samples at a known distance from a gamma-radiation counter, or, if greater sensitivity is required, by "liquid counting" of tissue extracts (Dobyns and Maloof, 1951). The ratio is useful as indicating whether the metastasis examined has any capacity to concentrate and retain radio-iodine. It does not estimate the relative doses of radiation that tumour and plasma would receive during radio-iodine therapy, since the plasma will usually receive its heaviest irradiation during the first day after the radio-iodine dose, which is then circulating as iodide; whereas the iodine-concentrating tumour will receive most of its irradiation in later days, from organically combined radio-iodine.

If the tumour radio-iodine concentration at, say, four days after the dose is many times the low value to be expected in the plasma, the tumour can be regarded as retaining iodine and as possibly suitable for radio-iodine treatment. If, however, the tumour concentration is about equal to that in plasma the tumour either does not concentrate iodine and is unsuitable for treatment or, possibly, as in a case discussed below, the tumour may concentrate but not retain the iodine. The latter type of case, which might be suitable for radio-iodine therapy, could be missed if the biopsy was made after an interval which was optimal in most other cases.

*"Thyroid ablation" is used to cover the destruction of all normal thyroid tissue either surgically or by therapeutic doses of radio-iodine.

In this respect daily external counts may therefore be more valuable than observations at biopsy on a particular day.

If tumour tissue is removed from the thyroid gland or from an adjacent area radio-iodine may be present in the material examined owing to inclusion of small remnants of normal thyroid tissue (Dobyns and Maloof, 1951) and be misinterpreted as indicating uptake in the tumour.

In a case of "Hashimoto's thyroiditis" the large, hard, and bulky gland had led to a tentative diagnosis of carcinoma. Four days after a test dose of radio-iodine a sample of tissue regarded as carcinomatous lymph node was removed from the posterior triangle of the neck and was found to be considerably more radioactive than a sample of muscle removed at the same time. Autoradiograms from this tissue, however, showed the radio-iodine to be present in islets of normal thyroid tissue displaced into the lateral cervical region by the growth of lymphadenoid tissue.

An autoradiogram is therefore likely to give more reliable information than simple radioactivity determinaations on tissue removed from the neck. It will also give evidence of the homogeneity of any radio-iodine uptake, and so of the uniformity of radiation to be expected.

Autoradiograms on Biopsy Material

The autoradiograms obtained from thyroid carcinomata have been discussed in detail by several authors (Dobyns and Lennon, 1948; Fitzgerald and Foote, 1949; Marinelli *et al.*, 1947; Rawson, Skanse, *et al.*, 1948), who have shown that iodine concentration occurs most commonly in well-differentiated tumours and particularly if colloid-filled follicles are present, or in those areas of an adenopapillomatous carcinoma in which such follicles occur. It has, however, been emphasized repeatedly that uptake is not always correlated with these or other histological structures. An autoradiogram may therefore be valuable in demonstrating the uptake that sometimes occurs in undifferentiated tumours of the thyroid. It can give direct evidence that a tumour, or at least the metastasis examined, may be suitable for radio-iodine treatment, although it will give no exact basis for calculating the radiation dose to be expected.

A negative autoradiogram should not be taken to exclude good prospects from treatment unless an adequately large test dose has been given, and the following calculation suggests that several millicuries may be required.

Radio-iodine treatment would certainly be worth giving for any tumour which would receive 5,000 r of beta radiation from a 100-mc. oral dose. But a radio-iodine autoradiogram would normally become positive only if the tumour retained an average of about 1 μc. per ml.; and tissue retaining 1 μc. of I^{131} per ml. will receive a total of about 150 r of beta radiation. But all tumours which will receive 150 r or more, and therefore give a positive autoradiogram, from a 3-mc. test dose should, on a proportionate basis, receive 5,000 r or more from a 100-mc. therapy dose. This calculation is inexact in several ways. It suggests, however, that a tumour which may respond to radio-iodine therapy will not necessarily give a positive autoradiogram after a test dose of only 1 or 2 mc.

The corresponding test dose could be very much smaller if the metastasis were remote from the thyroid, so that it was unnecessary to use an autoradiogram to show that any uptake observed was in the tumour and not in normal thyroid tissue contained within the biopsy material. With a test dose of only 150 μc., 1 g. of a tumour removed at biopsy and of the activity considered above would contain 0.05 μc., which could be readily measured by a gamma counter. Liquid counting of an extract from this weight of tissue would determine accurately a content of 0.004 μc., which would be achieved with an even smaller test dose of 12 μc.

It is evident that autoradiography will give valuable evidence in the selection of cases for radio-iodine treatment, provided that an adequate test dose of several millicuries is given; and much smaller test doses can be used if an autoradiogram is unnecessary. In many cases, however, this direct evidence may be unobtainable because of difficulties in biopsy or serial biopsy, or possibly because of rapid discharge of iodine from the tumour; and selection of cases may then depend upon external counting methods. These methods have great practical value throughout the investigation of thyroid carcinomata and are always essential in the control of treatment.

External Counting

Since its gamma radiations penetrate body tissues freely, radio-iodine within the body can be detected by a counter external to the body; and its localization within the body can be examined if the counter is suitably shielded so as to receive radiations from certain known directions only. Two such types of shielding are found to be useful. If the counter is surrounded by a cylindrical lead shield which is open at one end only (Fig. 1), this open end can be placed on or over the body surface at any point, and the counter used to determine the amount of radio-isotope underlying the surface at that point (Corbett and Honour, 1951). In this way a chart may be constructed showing the distribution of radio-iodine in any body region (Pochin, 1950; Coliez *et al.*, 1951). This method, which may be described as "local counting," has been widely used in exploring the body for iodine-concentrating metastases (Frantz *et al.*, 1944; Dobyns and Lennon, 1948; Seidlin *et al.*, 1949; Pochin, 1950; Green *et al.*, 1951).

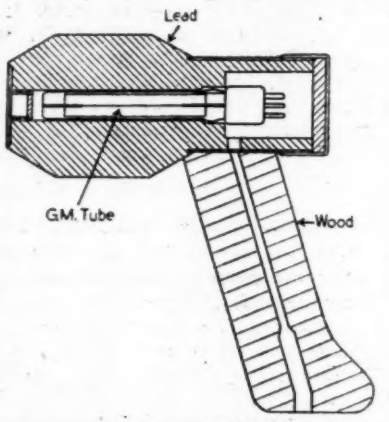

FIG. 1.—Counter shielding applicable to "local counting."

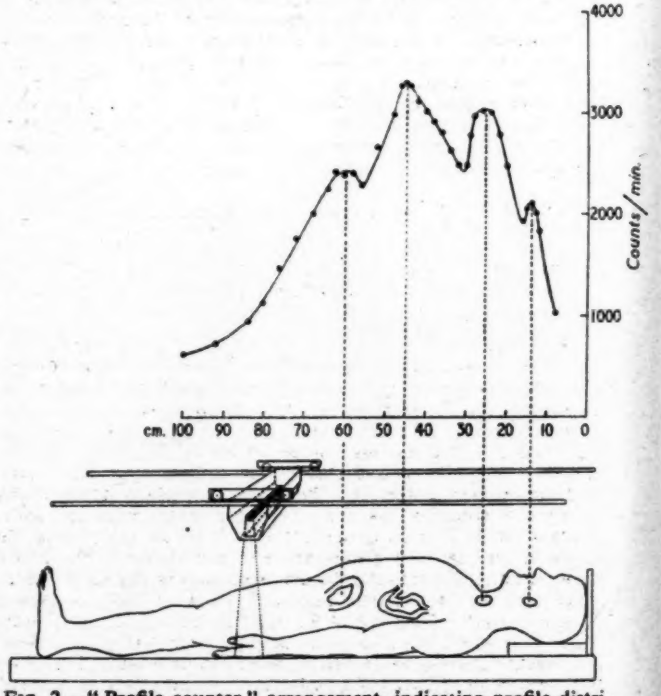

FIG. 2.—"Profile counter" arrangement, indicating profile distribution observed in a case of thyroid carcinoma, with peaks of uptake corresponding to bladder, stomach, carcinoma tissue in the neck, and salivary glands. Case 17.

Alternatively, the counter may be shielded by lead plates on each side of it and used to estimate the distribution of radio-iodine along the length of the body. By making counts with such a counter at different positions down the anterior midline of the body (Fig. 2) a diagram can be constructed showing the radio-iodine content of the tissues at each level examined. The diagram gives a "profile" of radio-iodine distribution down the body which may be of considerable value in detecting and following uptake in metastases (Pochin, 1950; Dobyns and Maloof, 1951).

The procedures of "local counting" and "profile counting" have somewhat different uses. An iodine-concentrating area in the body will often be detected with greater sensitivity and efficiency by the profile method, and the affected tissue or organ then be identified by local counting over the suspected area and, if necessary, with a larger test dose. Subsequent variations in the radio-iodine content of the tissue so localized will, however, often be more accurately measured by the further use of profiles than by local counting, since the counting rates measured with any highly directional local counter depend critically on the exact position and orientation of the counter relative to the body, which are less easily controlled than with a profile counter.

Metastases Remote from any Iodine-concentrating Tissues

When a metastasis is remote from the thyroid or from any other tissue in which iodine is normally concentrated, either counting procedure is likely to give clear evidence of uptake in any tumour in which the uptake is adequate to allow effective radio-iodine treatment. Thus, a metastasis comprising only 2 g. of tumour tissue with enough uptake to receive 5,000 r from a 100-mc. dose would be readily detected by a gamma-radiation counter 20 cm. from it after a test dose of 1 mc., if it was remote from other iodine-concentrating tissue. The problem in external counting is, in fact, usually one of *discrimination* rather than of *detection* of sites of radio-iodine concentration. Difficulty may, however, arise with very small metastases or in detecting weak uptake which is insufficient to allow immediate treatment yet might indicate the value of further treatment designed to increase such uptake.

Usually in such cases the concentration of radio-iodine may be identified by comparing counts over the tumour with those at surrounding points or on the opposite side of the body. Over a large metastasis in the femoral neck from a thyroid carcinoma, however, we have observed counts between 1.7 and 3 times those over adjacent areas or over the opposite femur. Since other metastases in this patient (Case 18) showed no radio-iodine concentration at biopsy, however, it seemed likely that the slightly raised counts over the femur were due to the increased size and perhaps vascularity produced in the thigh by the metastasis.

Metastases Adjacent to Iodine-concentrating Tissue

Greater difficulties arise when the tumour lies near tissue which normally concentrates iodine, and a familiarity with the sites and times of such normal concentration is essential in the diagnosis of uptake in tumours.

When radio-iodine is given as iodide it normally circulates in the blood stream for two or three days, its concentration decreasing as it is progressively removed by the thyroid and kidneys. In myxoedema or in renal failure this initial phase of circulating radio-iodide may be demonstrable for up to six days, whereas in thyrotoxicosis it is usually completed within 12 hours. During this phase the kidneys and bladder will contain radioactive urine, and the bladder content of radio-iodine is regularly demonstrable by suitable counting methods. Since the gastric juice and saliva contain iodide in high concentration relative to the plasma, the stomach and salivary glands are also radioactive. The gastric concentration is commonly demonstrable during this iodide phase, even after an intravenous dose. The radio-iodine in salivary glands is usually detectable at the same period only in myxoedema, since otherwise the radio-iodine in the adjacent thyroid prevents the weaker salivary uptake from being discriminated. The radio-iodine content of the milk of a lactating breast would also usually be detectable.

Within a few days of an oral or intravenous dose almost all the administered radio-iodine will have entered the thyroid or been excreted in the urine. After this time, renal, gastric, or salivary uptake continues only at a very much lower rate, depending upon the recirculation of small quantities of radio-iodine that have completed the metabolic iodine cycle. These small amounts are not usually detectable, but might give difficulty in cases with rapid iodine recirculation. Normally, however, by a few days after the dose radio-iodine can be detected only in thyroid tissue or in such thyroid tumours as concentrate and retain iodine. As, however, at this stage thyroxine containing radioactive iodine is being released by the thyroid, any site of high thyroxine concentration may become detectable by external counting. The liver appears to be readily detectable in this way (Pochin, 1950) provided that the blood radiothyroxine content is high enough. This occurs commonly after a few days in hyperthyroid subjects, but we have rarely seen it in normal subjects with present methods of examination, and then only a week or more after the dose. It is possible, however, that in patients with functioning thyroid tumours the liver radiothyroxine content may be detectable by external counting and be mistaken for uptake in pulmonary or other metastases at this level. The radio-iodine content of the liver may also be conspicuous during destruction of the thyroid gland by radio-iodine, when organically bound radio-iodine is being discharged rapidly into the circulation.

In tumours adjacent to the bladder, kidneys, stomach, or salivary glands, therefore, any radio-iodine uptake that occurs may be difficult to detect in the first few days after the dose but will usually be evident thereafter. In tumours adjacent to the liver, uncertainty will occur only if organically bound iodine is being discharged rapidly from the thyroid, as may be established by plasma samples. In tumours adjacent to the thyroid, however, the difficulties are always greater, since normal thyroid tissue takes up iodine rapidly and retains it for long periods.

Metastases Close to the Thyroid

In some patients with tumour tissue only in or adjacent to the thyroid, the detection of uptake may prove impracticable by external counting. In such cases local counting may indeed show that the normal uptake of a thyroid lobe invaded by tumour is much reduced, and indicate that the tumour does not concentrate iodine with an efficiency approaching that of thyroid tissue. Slight remaining activity in the lobe may, however, be due to some remaining thyroid tissue or to weak tumour uptake. The distinction between these two possibilities is important in the selection of cases for treatment, yet cannot usually be made by external counting.

Occasionally, however, local counting may be useful in showing that the distribution of radio-iodine in the neck closely follows the outline of tissue masses regarded as being neoplastic. This result may be due simply to generalized expansion of the thyroid—for example, in thyroiditis—but if the masses are shown to be carcinomatous by biopsy it may give a strong indication that they concentrate radio-iodine (Fig. 3). Normally, however, in any tumour adjacent to the thyroid, uptake can be tested adequately only after total thyroid ablation, which is in any case a necessary step if radio-iodine treatment is attempted.

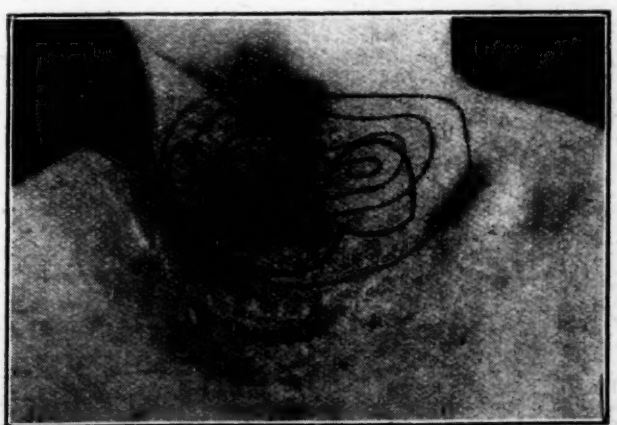

FIG. 3.—Outline of palpable carcinomatous mass in neck (continuous line) and corresponding contours (interrupted lines) indicating underlying concentrations of radio-iodine. Case 3

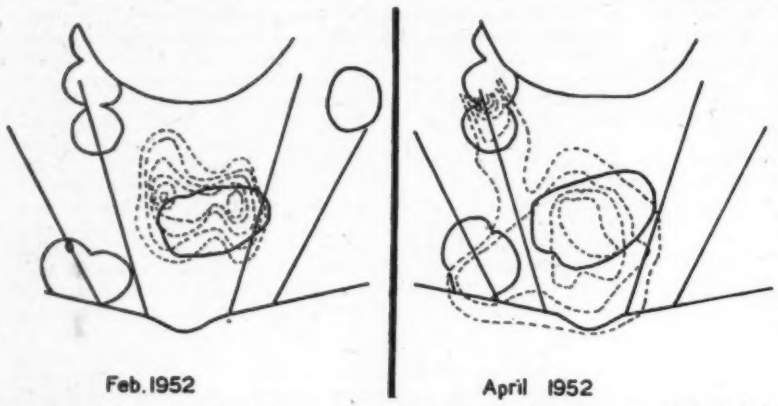

FIG. 4.—Areas of radio-iodine concentration in the neck: February, 1952, before thyroid ablation, indicating uptake in both thyroid lobes, but not in metastasized lymph nodes; April, 1952, after thyroid ablation, uptake in glands now being apparent. Case 8.

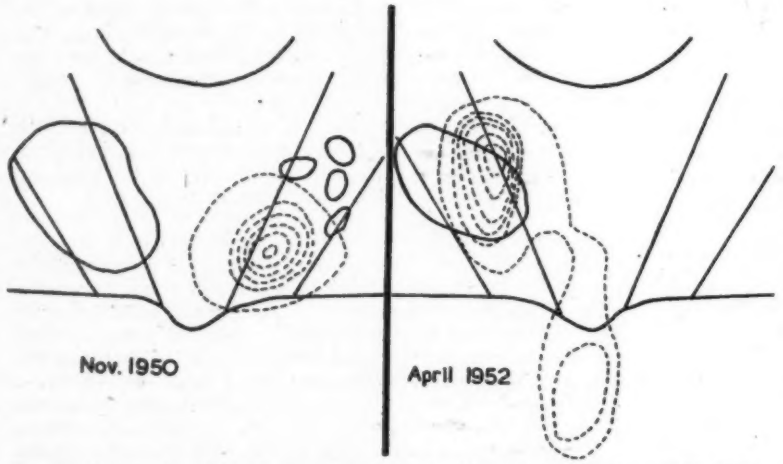

FIG. 5.—Areas of radio-iodine concentration in the neck: November, 1950, before thyroid ablation, suggesting uptake in remaining left thyroid lobe but not in right-sided mass deep to sternomastoid; April, 1952, after thyroid ablation, uptake now evident in right-sided mass and probably also in mediastinal glands. Case 5.

Effects of Thyroid Ablation

As has been mentioned, radio-iodine uptake in a thyroid carcinoma may only become demonstrable after all normal thyroid tissue is removed from the body. This might be due to any of several causes:

(1) The amount of isotope concentrated by the tumour will be greater when it is competing for radio-iodine against the kidneys alone, and not against kidneys and the normal thyroid. The uptake will normally be about doubled after thyroid ablation owing to this effect.

(2) The detection of weak uptake is technically simpler if no site of strong uptake such as thyroid tissue is adjacent. This is a most important consideration with metastases in the neck, and, except with heavily shielded counters, may sometimes apply in the case of mediastinal or pulmonary metastases.

(3) In certain cases the capacity of the tumour to concentrate iodine seemed to develop only after thyroid ablation; or in other cases to have increased under these circumstances (Rawson, Marinelli, *et al.*, 1948; Rawson *et al.*, 1949; Dobyns and Maloof, 1951).

Thyroid ablation has been of value in revealing or inducing iodine uptake for the first time in five of our cases of thyroid carcinoma. In three, uptake then became demonstrable in metastasized glands at the angle of the jaw (Cases 8 (Fig. 4) and 9) or below the sternomastoid (Case 5, Fig. 5); while in two other patients uptake could be detected in mediastinal (Case 6, Fig. 6) or pulmonary (Case 4, Fig. 7) metastases.

The cases are quoted to show the practical necessity for thyroid ablation in detecting cases which may be suitable for radio-iodine treatment. They do not prove that uptake in the tumour was induced or increased, rather than simply revealed, by thyroidectomy. This important distinction may be made when, after thyroid ablation, the tumour uptake increases progressively (Rawson, Marinelli, *et al.*, 1948). It could be systematically examined if the plasma radio-iodide clearance rate of the tumour or of a metastasis is measured before and after a thyroid ablation, and this has not been reported. Some estimate, can, however, be made, if the renal clearance for

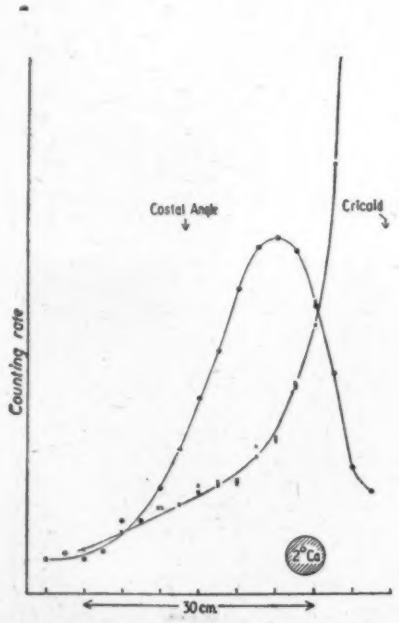

FIG. 6.—Profiles showing: before thyroid ablation (crosses), uptake in thyroid region only; after radio-iodine ablation (dots), clear uptake corresponding in position to mediastinal mass. Case 6.

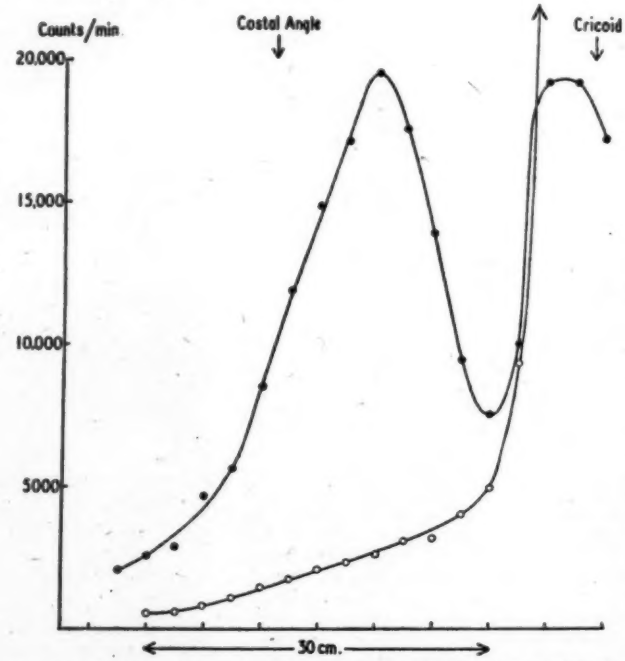

FIG. 7.—Profiles showing: before thyroid ablation (open circles), uptake in thyroid region only; after thyroidectomy (dots), clear uptake corresponding to pulmonary metastases as well as to remaining thyroid tissue in neck. Case 4.

iodide is assumed to be unchanged, or is estimated, before and after ablation; and if the tumour uptake is compared with the proportion of the dose initially excreted in the urine (Dobyns and Maloof, 1951).

Frequency of Demonstrable Uptake

The frequency of radio-iodine uptake may be illustrated by the findings in 27 patients examined by these methods in the last four years (Table I). Only those cases are

TABLE I.—*Radio-Iodine Uptake in Tumour Demonstrated Before and After Thyroid Ablation*

Histological Type	Case No.	Before Ablation	Thyroid Ablation Effected by	After Ablation	Plasma Concn.† %/l.
Adenocarcinoma	1	Clear	Surgery	Clear	2·2
Papillary adeno-carcinoma	2	None	Not attempted	—	0·3
	3	Probable	Radio-iodine	None	—
	4	None	,,	Clear	—
	5	,,	,,	Probable	0·3
	6	,,	,,	Clear	0·7
	7	,,	Not attempted	—	—
	8	,,*	Radio-iodine	Clear	0·5
	9	,,	,,	,,	0·8
Adenocarcinoma becoming anaplastic	10	,,	Not completed	—	0·03
	11	,,	Not attempted	—	—
	12	,,*	Not completed	—	—
	13	Clear	Surgery	Clear	0·05
Papillary carcinoma, some follicles	14	None	Radio-iodine	None	0·1
	15	,,	,,	,,	0·1
	16	Probable	,,	Probable	0·6
Anaplastic, some follicles	17	Probable	Radio-iodine	Probable	0·5
	18	None	,,	None	0·06
	19	,,	Not attempted	—	0·6
Anaplastic	20	,,	,, ,,	—	—
	21	,,	,, ,,	—	—
	22	Probable	Seen too late	—	—
	23	None	Radio-iodine	None	—
	24	,,	,,	,,	—
	25	Not seen	Surgery	Probable	0·02
	26	None	Not attempted	—	—
	27	,,	Seen too late	—	0·05

* Metastasized cervical glands became tender and reduced in size following the ablation dose of radio-iodine.

† The plasma concentration indicates the maximum or limiting concentration of protein-bound radio-iodine, in % of the dose per litre, reached after doses given early in the treatment. With effective treatment the concentrations so attained fall progressively with successive doses.

included in which the tumour structure has been examined histologically from the primary or at least one metastasis, and has indicated malignant disease consistent with a thyroid carcinoma. All patients so diagnosed have been included except two who have been seen only recently. Table I indicates the histological type of carcinoma, the type of any thyroid ablation performed, and whether radio-iodine uptake was observed in the tumour by external counting methods either before or after ablation.

It will be seen that in the 26 cases examined before thyroid ablation radio-iodine uptake was clearly demonstrable in two and was probable but not certain in four more. In the remaining 20 no uptake could be demonstrated at this stage, although in seven there were metastases remote from the thyroid. The thyroid was then ablated, surgically or by radio-iodine, in five of the patients in whom uptake had been proved or suspected, and in 10 of those without demonstrable uptake; and it had already been removed before the first examination of a further case. After ablation in these 16 patients, or during subsequent radio-iodine therapy, conclusive evidence of uptake was obtained by counting methods in a total of six cases, with probable uptake in four more; uptake was indicated in one further case (No. 12) by considerable tenderness and reduction in size of enlarged submental glands during radio-iodine ablation; and in at least one other case the absence of uptake after ablation was associated with a diminution in the tumour mass and may have been due to tumour destruction.

Radio-iodine uptake has thus occurred in at least a quarter of all patients and probably in over one-third. Of patients with mainly differentiated tumours examined after ablation, uptake has been demonstrable in over one-half with certainty and probably in about three-quarters (Table II).

TABLE II

Group	Radio-iodine Uptake				Proved or Probable
	Proved	Probable	Not Shown	Total	
All tumours seen	7	6	14	27	48%
All differentiated tumours ..	7	3	6	16	62%
All differentiated tumours after ablation ..	6	2	3	11	73%

These frequencies cannot be taken as representative of all thyroid carcinomata, since many of our patients were sent for investigation on the understanding that histologically differentiated tumours were most suitable for treatment; and uptake has been demonstrated less frequently in other series of cases (Frantz *et al.*, 1948; Dargent *et al.*, 1950; Paterson, 1950; Dobyns and Maloof, 1951; Green *et al.*, 1951; Rawson *et al.*, 1951—but see Marinelli *et al.*, 1947; Seidlin *et al.*, 1949; Coliez *et al.*, 1951). On the other hand, several patients with differentiated tumours might have shown uptake if examined after thyroid ablation.

It seems clear that a significant proportion, at least of differentiated thyroid carcinomata, can be shown to concentrate radio-iodine to a useful degree, and particularly if normal thyroid tissue is first ablated.

Evidence of Tumour Function from Plasma Radio-Iodine Concentration

Thyroid carcinomata rarely liberate enough thyroxine to cause clinically evident thyrotoxicosis. In one of our patients (Case 1) the large and multiple pulmonary metastases of highly functional tissue did cause a typical thyrotoxicosis, which was abolished after radio-iodine destruction of tumour tissue (Pochin, 1950). This degree of activity is, however, too unusual to be of value in diagnosing iodine uptake in a tumour. A more sensitive test may be based upon the rate with which protein-bound radio-iodine accumulates in the plasma after a dose of radio-iodine. Its concentration usually rises during the first few days to a "plateau" value of which the height probably indicates the rate of thyroxine production in the body (Pochin, 1950). Seidlin *et al.* (1951) observe that in cases of thyroid carcinoma the value attained has some correlation with function in the tumour. This relationship is evident from Table I, the three highest values occurring in patients with iodine-concentrating tumours. The correlation, however, is not exact, since at least one of our cases with clear although probably transient uptake, and a good response to treatment, has shown a low plateau value (Case 13). It seems probable, however, that useful indications of the presence of functioning tumour tissue would often be obtained if this test was made under standard conditions—for example, by measuring the protein-bound radio-iodine six days after a 1-mc. test dose given after thyroid ablation in a patient who was not receiving thyroxine.

Evidence of Tumour Function from Urinary Radio-Iodine Excretion

The urinary excretion of a test dose of radio-iodine gives indirect and approximate evidence of the presence of iodine-retaining tissues in the body. Thus if any greater proportion than about 10% of the dose remains unexcreted after, say, four days, it is likely that thyroid or functioning tumour tissue is still present. More direct and valuable information could, however, always be obtained by examining the localization of this retained radio-iodine by profile measurements, except possibly if tumour tissue were widely disseminated. The urinary excretion is also useful in estimating the radiation dosage that the body as a whole will receive.

Some basis for this estimate may be derived as follows. Most of the whole body radiation will be received while the radio-iodine is circulating as iodide rather than as thyroxine, except when much functioning tissue is present. As a rough approximation, the dose (d) of radio-iodine may be regarded as causing a plasma concentration which then falls exponentially with a half-period inversely proportional to the sum of the renal iodide clearance (r) and the total iodide clearance (G) of thyroid and tumour tissue (Pochin, 1950). The plasma beta radiation from circulating radio-iodide will therefore be proportional to $\frac{d}{G+r}$; and the proportion of the dose initially excreted in the urine will be given by $\frac{r}{G+r}$. For a given radio-iodine dose (d) and with a normal renal clearance (r), the body radiation will therefore be approximately proportional to the urinary excretion of the dose, whatever the value of G. Since, however, the value of G rarely exceeds that of r, the body radiation per millicurie is unlikely to change by a factor of more than two even after the thyroid has been totally ablated.

The urinary excretion may therefore be informative when a large tumour of poor uptake is being treated, since whole body radiation will be a limiting factor in treatment and it is important that the ratio of tumour to body radiation shall be high for every dose; and if the dose is largely excreted in the urine little will remain in and irradiate the tumour. For a tumour which is not decreasing in size, therefore, therapy should be avoided if the tumour uptake of iodine is low and the urinary excretion high. If, however, the tumour retains good uptake but is decreasing in size, the remaining tumour tissue can be irradiated with little loss of efficiency even though the urinary excretion is high.

Other Indications of Radio-iodine Uptake

In two patients a therapeutic dose of radio-iodine has caused clear and severe tenderness in metastasized lymph nodes, although it had not been possible to demonstrate uptake in these nodes by counting methods during a preceding test dose or after the therapy dose. Similar tenderness is normally observed during the week following the dose in the thyroid gland during radio-iodine ablation if doses of 60 to 100 mc. are used; and is presumably due to irradiation injury. When it occurs in neoplastic tissue it may therefore be taken as evidence of radio-iodine uptake. This interpretation was supported by a considerable reduction in size of the lymph nodes concerned in both cases and by other evidence of uptake: in one case by external counting eight weeks after ablation, when the remaining palpable metastasized glands concentrated well; and in the other by histological evidence of tumour destruction in the glands concerned. In each case normal thyroid tissue was still present in the neck and adjacent to the glands concerned, which may account for detection of uptake by tenderness and not by counting. Such tenderness may thus give the first indication that uptake is occurring. Oedema may also develop at the site of the tumour during radio-iodine therapy. We have observed this in one case with metastases in glands of the posterior triangle and in another patient with pulmonary metastases involving the pleura who developed a moderately extensive although transient pleural effusion on the side of the lesion within five days of the first therapeutic dose.

It seems likely, therefore, that the occurrence of local pain or oedema during the week after a therapeutic dose may support or extend the evidence of uptake; and that in some cases these events may provide a more sensitive, although less objective, indication of such uptake than measurements over the tumour.

Procedure in the Investigation of Thyroid Carcinoma

Since none of our patients have been under radio-iodine treatment for longer than three and a half years, no general statement can be made on its efficacy. It is, however, clear from the response of certain of our patients (Pochin, 1950) and of cases previously described (Howes and Foote, 1949; Horn and Ravdin, 1951; Sorrentino *et al.*, 1951) that the treatment can be valuable, and probably curative in some patients (Seidlin *et al.*, 1951) even when metastasis has occurred before radio-iodine is given. It is also clear that it can be effective in a significant proportion of all thyroid carcinomata, and not only in occasional cases. Finally, it seems that treatment may be valuable for a tumour which cannot by the usual counting methods be shown to concentrate radio-iodine before thyroid ablation.

When a thyroid carcinoma is diagnosed, therefore, it is usually necessary to decide, without evidence that the tumour concentrates iodine, whether the normal thyroid tissue should be removed. This decision will normally be based on the histology of the tumour, since it has been shown that the most differentiated tumours, and particularly those with abundant colloid, are likely to concentrate iodine, although the correlation between uptake and histological differentiation is not exact. This is supported by the results in our cases (Table I).

We therefore suggest the following procedure in the management of thyroid carcinomata:

1. Biopsy, if this seems surgically justifiable, for evidence both of the thyroid origin of the neoplasm and of its degree of differentiation; with

2. Radical excision if ever this course appears likely to be successful. If such excision is attempted and is found to be impracticable, and if biopsy has revealed a differentiated tumour, as much normal thyroid tissue as possible should be removed at this operation instead.

3. Inoperable tumours that are undifferentiated and seem likely to be radio-sensitive should be treated by radiotherapy if sufficiently localized and unless they have been shown to take up radio-iodine.

4. For inoperable but histologically well-differentiated tumours, and certainly for those with colloid-filled follicles throughout their structure, thyroid ablation should be effected: (*a*) by surgical total thyroidectomy if possible, or (*b*) by radio-iodine in therapeutic (for example, 80 mc.) dosage. For completely anaplastic and rapidly growing tumours thyroid ablation is unlikely to be justifiable.

5. After thyroid ablation radio-iodine treatment should be instituted if adequate uptake can be detected in the tumour or induced, for example by use of thiouracil (Rawson *et al.*, 1951; Rall *et al.*, 1951). Therapy is continued until profile counting after a test dose reveals no abnormal site of radio-iodine retention, if this can be achieved without the development of radiation anaemia.

This scheme is clearly oversimplified in several respects, and the problems involved have been fully discussed by several authors (for example, Dobyns, 1951; Mitchell, 1951; Rawson *et al.*, 1951). It appears to afford a useful basis, however, for the initial selection of cases. In particular, it may have practical value in hospitals which are not at present using radio-iodine, since the most important steps in selection of cases for this treatment are independent of the use of isotopes. In patients with metastases remote from the thyroid, radio-iodine tests may be usefully made at any stage, but in tumours with colloid-filled vesicles these would in any case need to be repeated after ablation. In the absence of metastases remote from the thyroid, radio-iodine tests are rarely profitable before thyroidectomy, except sometimes when the tumour is extensive and thyroiditis can be excluded. For most patients, therefore, no information is lost, and valuable time may be gained, if a biopsy is performed immediately upon a presumptive diagnosis of thyroid carcinoma, and followed by total thyroidectomy if the tumour proves to be highly differentiated, the patient then being sent for radio-iodine investigation of residual areas of iodine uptake by profile counting. If thyroidectomy is impracticable, such a patient is sent for radio-iodine destruction of the thyroid, followed by treatment of any areas of abnormal concentration that are subsequently detected.

Finally, it should be emphasized that this procedure is suggested at an early stage in a form of treatment which will certainly develop considerably. Throughout this paper we have discussed methods of diagnosing tumours which concentrate *and retain* radio-iodine. A thyroid carcinoma might, however, concentrate radio-iodine in the tumour cells and convert it into organic combination but discharge it again rapidly, as would be likely to occur in the absence of

follicles. It should then show high initial uptake of radio-iodine for the first hours or day after the dose, which might allow its treatment by special methods. But it would have lost its radio-iodine by the second or third day, at which time autoradiograms and external counting tests of uptake are normally made. This might conceivably be the reason why most "undifferentiated" tumours—namely, those lacking follicles and colloid—are found to contain no radio-iodine when tested by normal methods several days after the dose. They may possess the biochemical cellular mechanisms and the capacity for uptake of iodine, even though they are shown not to have the follicular mechanism and capacity for its retention.

Dobyns and Maloof (1951) mention such behaviour in a metastasis in one case. We have had one patient (Case 13) in whom this mechanism of uptake and rapid discharge seemed to occur, and who has shown an unequivocal radiological response to treatment. The counting rate over the tumours, which were at the right lung base on the antero-lateral aspect of the chest, rose to a high value on the day following the dose. In the next two days the value fell progressively, and was almost zero after three days although normal thyroid tissue, remaining after thyroidectomy, had taken up radio-iodine progressively during these days (Fig. 8). This is the behaviour to be expected on mathematical grounds if the iodine storage time in the tumour is short, the mean time of stay having been only 2.3 days in this case. The estimation of the tumour uptake and discharge of radio-iodine, however, involves careful differentiation between activity ascribed to the tumour and that ascribed to viscera such as the stomach, the radio-iodide content of which is considerable soon after the dose. The distinction could not be made adequately by profile counting, since the levels of tumour and stomach did not differ widely.

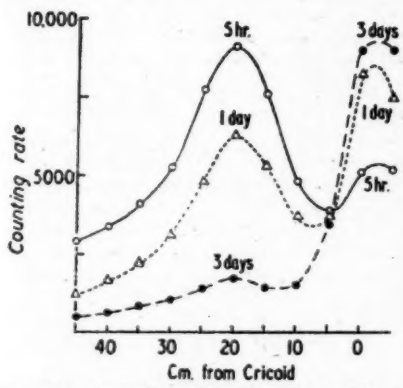

FIG. 8.—Profiles at intervals after radio-iodine in case of thyroid carcinoma with pulmonary metastases, showing initial uptake but rapid discharge in position corresponding to site of metastases. Case 13.

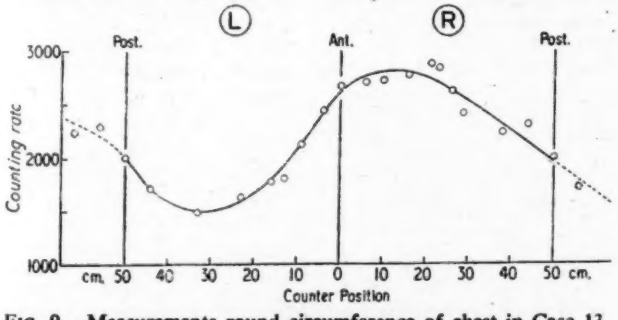

FIG. 9.—Measurements round circumference of chest in Case 13, showing uptake anteriorly and to the right, in position of metastases.

Measurements round the circumference of the trunk, however (Fig. 9), showed the highest counts to be opposite the site of the metastases and remote from that of the stomach. The evidence from this case is not conclusive, but it strongly suggests that a therapeutically useful degree of radio-iodine concentration in undifferentiated tumours may be unnoticed unless accurate and early profile examinations are made. It is clearly important that evidence of any such early uptake should be sought in this way in cases of undifferentiated thyroid carcinoma which have metastases remote from the bladder, stomach, or salivary glands. If uptake is found at this stage, and suitable treatment can be based on this finding, the criteria for selecting cases for thyroid ablation will clearly require revision, and the scope of radio-iodine treatment for thyroid carcinoma will increase.

Already, however, it appears essential that, with any inoperable thyroid carcinoma in which copious colloid is demonstrable microscopically, radio-iodine uptake should be investigated after total thyroid ablation. If this is not done it seems clear that a substantial proportion of these patients will be inadequately treated.

Summary

In at least one-quarter, and probably in over one-third of a series of patients with thyroid carcinoma, the tumour could be shown by external counting to take up radio-iodine. These methods, particularly by profile counting, are valuable in detecting and following the degree of such uptake, which may become apparent only after thyroid ablation.

It seems likely that all patients in whom biopsy reveals a well-differentiated thyroid carcinoma which cannot be removed surgically should be investigated with radio-iodine, preferably after thyroid ablation. In a substantial proportion of such patients radio-iodine may be useful in treatment even though the tumour has already metastasized.

We are greatly indebted to the many clinicians who have sent us these patients, to Dr. R. C. F. Poynton for his help in their care, and to Miss M. Adams, Miss J. Forshaw, and Miss E. Ryan for assistance in their investigation.

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Six films dealing with accessible cancers have been made by the Ministry of Health. They are intended for general practitioners and other professional audiences. They do not stress any particular method of treatment, but emphasize the added years of normal useful life which may result from early diagnosis and treatment. The regions covered are the skin; lip, tongue, and mouth; larynx; breast; cervix and uterus; and rectum. The Ministry has also revised the leaflets "Health" and "Medicine and Surgery," describing the films available on these topics and the terms on which they may be hired or purchased. All the films are available from the Central Film Library, Bromyard Avenue, London, W.3, or from 16–17, Woodside Terrace, Glasgow, C.3, or 48, Park Place, Cardiff.

THE EARLY STAGES OF THYROID CARCINOMA

BY

M. DARGENT, M.D.

AND

P. GUINET, M.D.

(From the Centre Professeur Léon Bérard, Lyons)

The relation between benign and malignant growth is not academic. If a malignant process can really arise within the capsule of a benign tumour, enucleation of the tumour should be a suitable method of prevention. But if, on the contrary, cancer occurs round a benign nodule more radical treatment is indicated.

Controversy is especially sharp in the case of the thyroid gland, as has been remarked by Brenizer and McKnight (1940). A clinician's opinion about degeneration in a goitre may be quite different from that of a pathologist. It is generally admitted in Europe by Swiss authors (de Quervain, 1940; Wegelin, 1926), as well as by German (Barthels, 1931), British (Dunhill, 1931; Joll, 1932), Russian (Kholdin, 1940), and French workers (Bérard and Dunet, 1924; Cuneo, 1938; Herbert, 1936; Velti and Huguenin, 1938), that carcinoma arises in a previous adenoma. American pathological opinion seems to be more divided. For instance, Pemberton in 1939 writes explicitly about cancer: "It arises either within an adenoma or from the portion of the gland free from adenomas. I believe that the latter origin is more common than the history would indicate." Even authors like Graham (1924) and Lahey, Hare, and Warren (1940), who admit that in general carcinoma arises in an adenoma, describe malignant growths occurring directly in apparently healthy parenchyma. Recently Cole, Slaughter, and Rossiter (1945) stated that only 37% of cancers arise in foetal adenomas.

We have collected aetiological data, experimental results, and pathological findings to prove that a true thyroid adenoma will probably never become malignant.

Before passing to a more detailed discussion we must give a better definition of an adenoma and a carcinoma. An adenoma is a true benign tumour, composed of follicles filled with colloid and a thick well-defined capsule, easily enucleated from surrounding tissues. Bielschowsky (1944) points out that such tumours are not influenced by pituitary thyrotropic hormone; they are subject to trophic disturbance—i.e., cystic degeneration, haemorrhage, and calcareous alteration. Surrounding hyperplasia may decrease or increase, but the adenoma will not alter unless vascular or trophic changes occur, and will be free from hormonal influence. According to Van Dyke and Miss Thelma Dunn (1944), there may be discovered in a gland congenital cysts with ciliated cells which are not true adenomas but will probably remain benign. Like most pathologists, we think that the so-called Wölfler's foetal adenoma is merely a form of hyperplasia—not a congenital tumour.

On the other hand, in practice we admit that there are four principal types of cancer: (*a*) the orthoplastic or differentiated cancers—namely, vesicular, trabecular, papillary types—and almost polymorphic ones which are papillary in some places and vesiculo-trabecular in others (so-called "Wucherndes" adenoma of Langhans), including also the Hürthle-cell tumours; (*b*) anaplastic growths, small- or large-celled; (*c*) spindle-celled tumours, very rare; and (*d*) sarcomas, including haemangioendotheliomas. These appear rather frequently in Switzerland, and we recently reported two cases (Dargent, 1947; Martin, Dargent, and Guinet, 1947).

One must admit that there is no clear dividing line between the less-differentiated vesicular or even papillary forms and undifferentiated or anaplastic ones. Spindle-celled forms may possibly be metaplastic.

Aetiological Data

The well-known relation between frequency of endemic goitre and that of carcinoma has been emphasized by Barthels (1931), Limacher, and McClendon (1939). Nevertheless, Klose and Helwig point out the low rate of carcinoma in the Main valley, where multinodular goitres are frequent. Bircher, in Argau, found 25 carcinomas for 1,425 goitres; and here, where 22 to 50% of children are goitrous, four cases of carcinoma were found in the two first decades: so-called papillary adenoma and the papillary carcinoma do not occur in previously goitrous glands. De Quervain thinks that such cases in Switzerland are probably imported ones. It is particularly striking to find that, in France, statistics for Paris and its surroundings (Velti and Huguenin) show 11 papillary tumours in 88 cases, while in the Lyons region, where endemic goitre is more important, we find only four typical cases out of 32. But endemic goitre is obviously disappearing everywhere, and these arguments become less and less valuable. Considerations of sex, age, and clinical history are more important.

Sex.—We tried to find a ratio, R, between the frequency of different types of thyroid disease in males and females, using 472 cases of goitre and 116 of carcinoma from 1934 to 1940 in the surgical departments of Professor Bérard and the Centre Anticancéreux (see Table).

Sex Ratio in Various Types of Thyroid Disease

	No.	Females	Males	R (approx.)
Graves's disease	113	106	7	15
Toxic goitre	81	71	10	7
Diffuse atoxic goitre ..	99	71	28	2·5
Nodular atoxic goitre ..	179	133	46	3
Orthoplastic carcinoma ..	56	33	23	1·5
Anaplastic carcinoma ..	60	36	24	1·5

R is particularly high for Graves's disease and less for diffuse atoxic goitres, the lowest ratio, 1.5, being obtained for the two principal forms of carcinoma. Many authors (Joll, Von Eiselberg, Eerland (in Java), and recently Cole, Slaughter, and Rossiter) have found figures of the same order. The nearest R to that of cancer is the value for diffuse atoxic goitre, in which sectioning may show micronodular nodes which are not true adenomas.

Age.—We have plotted several graphs of frequency of disease at different ages. Well-known facts appear: for instance, Graves's disease has two peaks—one in puberty, and one in the menopause in the female. The average age for toxic adenoma is slightly later. For diffuse atoxic and nodular goitres the graphs are less interesting on account of difficulty in ascertaining the exact time of onset of the disease. If carcinoma can arise in a pre-existing adenoma the average age for malignancy should be later; this is true for anaplastic forms occurring mainly after 60 years. However, it is important to point out that in our group of cases only 24 of 61 patients with the anaplastic form had previously had a goitre. On the contrary, it is obvious that the average age for the orthoplastic forms of cancer is the same as for goitre (Figs. 1 and 2)—Pemberton and Lovelace (1941) and Cole, Slaughter, and Rossiter (1945) agree with us on this point—and the frequency of such carcinoma in childhood and youth is even comparable with

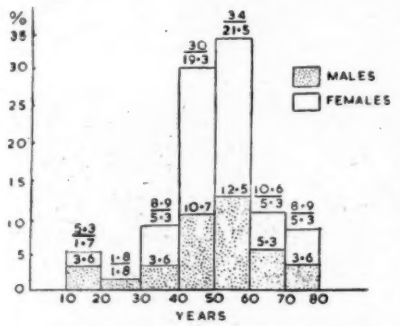

FIG. 1.—Average age for the orthoplastic forms of carcinoma of the thyroid.

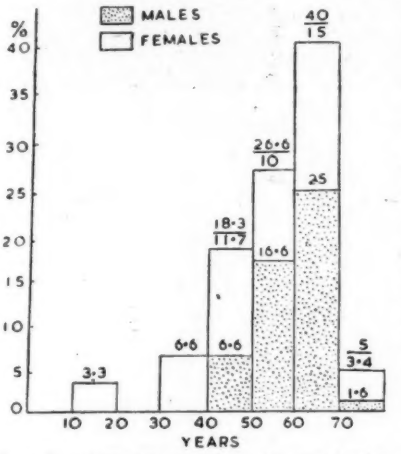

FIG. 2.—Average age for the anaplastic forms of carcinoma of the thyroid.

the frequency of benign growth. (These findings are very similar to those of Taylor and Wilkinson (1935), Pemberton, and Black.) If we admit that in the first two decades of life two types of thyroid hyperplasia may be met—namely, the atoxic and the toxic—we should add a third type which might be called "malignant hyperplasia," and, according to our figures, the chances of each up to the age of 20 years would be: atoxic parenchymatous hyperplasia, 8.6%; toxic hyperplasia and toxic goitre, 6.1%; so-called malignant hyperplasia, 4.3%.

Clinical History.—Having witnessed the slow evolution of most of the orthoplastic forms, especially papillary and vesicular, we agree with Velti and Huguenin that if a goitre appears in less than eight years from the first complaint one must think the tumour malignant from the first. Having carefully gone through the observations of Lahey on cancer in adenomas, we wonder if goitres developing in two, three, or four years, or as little as 10 months, were not always carcinomas. In our view one cannot be sure of the degeneration of an adenoma unless it has existed for 8 or 10 years, and on this criterion we find that only 50% of carcinomas arise in a previous goitre, as already ascertained by Bérard and Dunet, Velti and Huguenin, and Müller.

Experimental Facts

The early work of Gaylord, Marine, and Lenhardt in 1910–11 showed a diffuse benign hyperplasia of structures throughout the gland submitted to stimulation, liable to regress if the stimulus stopped. But if the stimulation had been long continued a true papillary adenoma might remain afterwards. These findings are most important, as Dunhill remarks, though they do not concern carcinoma. Bielschowsky's experiments in 1944–5, however, give very important data on the occurrence of thyroid carcinoma. Briefly, he states that malignant growths may occur in a parenchyma treated with allylthiourea and simultaneously with a known carcinogenetic agent—namely, *o*-aminofluorene. The adenocarcinomatous nodules escaping through their capsules do not arise in previous simple adenomas, which appear only in animals fed for a long time with allylthiourea alone. Similar facts have been described by Griesbach, Kennedy, and Purves (1945).

If, at first, thiourea or *Brassica* seeds bring on a simple hyperplasia, this hyperplasia gives way later to a well-defined adenoma. Simultaneous addition of a carcinogen such as *o*-aminofluorene may convert this hyperplasia to a malignant growth instead of a benign one. We cannot say whether the association of a thio- group with the carcinogen is really necessary.

Morris, Dubnik, and Dalton (1946), as well as Gorbman (1946), have found metastases of normal thyroid tissue after a long treatment with thiourea and thiouracil. In spite of the benign pattern of these formations, here is thyroid hyperplasia with blood-stream invasion. Is it really malignant? This is the general problem of the so-called benign metastatic adenoma.

Our opinion is that such growths are already malignant, and are not adenomas. They are malignant nodules as different from true adenomas as are colloid lobulated nodules. This has been well emphasized by Warren (1947). Clinical facts such as the case report by Payne, Crane, and Price (1947) of a malignant process arising in a patient with Graves's disease during treatment with thiouracil are as valuable as experimental results.

In brief, we think that somehow a previously healthy thyroid parenchyma, with or without an old benign adenoma which is the sign of a previous wave of benign hyperplasia, undergoes a special type of hyperplasia when treated with thiourea and carcinogen, or perhaps even with a thio- compound alone. We suggest it should be called malignant hyperplasia. The simplest form is perhaps the so-called benign metastatic adenoma which Bérard and Dunet named appropriately "adenomorphic carcinoma."

Adenocarcinomatous papillary, follicular, and even trabecular nodules seeming to arise in a foetal adenoma are a lobulating form of this hyperplasia. The most severe form is the anaplastic. In all these cases the rupture through the capsule—well shown in Goetsch's (1940) photomicrographs—and invasion of blood or lymphatic vessels are the first two signs of the malignant nature of the growths (Graham, 1924).

Pathological Studies

In several cases we found entirely independent adenomatous and carcinomatous lesions. Autoradiographic plates, obtained after administration of I^{131} in unpublished recent cases, show the accuracy of such a distinction.

A. The Boundary Between Adenoma and Cancer

Case 1.—A man aged 32, suffering from goitre since the age of 30. Pain in the neck, hardening and increasing volume of goitre, voice becoming hoarse; wasting and fever appeared three months before. Physical examination showed a hard mass in the right pole of the thyroid. Straightforward thyroidectomy under local analgesia. It was obvious, however, that a part of the growth passed down into the mediastinum along the internal jugular vein. Post-operative *x*-ray treatment, 6,000 r. Death occurred six months later from acute dyspnoea caused by mediastinal metastasis. Pathological examination showed a well-encapsulated, lighter-tinted, softer nodule the size of an apricot, lying in the centre of a diffuse carcinoma, from which it was separable with the finger. Microscopically, there was centrally a small- to medium-sized follicular adenoma with endotheliform epithelium, some follicles being empty, some

FIG. 3.—The borderline between an anaplastic cancer and an adenoma. The malignant growth has invaded the capsule from outside.

filled with more or less eosinophilic colloid. A definite boundary could be made out between these adenomatous follicles and the atypical carcinoma surrounding it and distorting the capsule at some points without involving it. The connective tissue all round the adenoma was scarlike, invaded by isolated or grouped neoplastic cells (Fig. 3).

Case 2.—A woman aged 78 had had a small "adenoma" for a very long time, with a severe illness recalling thyroiditis in the last month. Examination showed the same pattern as in Case 1. The adenoma was calcareous in the centre and rubber-like more peripherally; atypical carcinoma had developed all around it (Fig. 4).

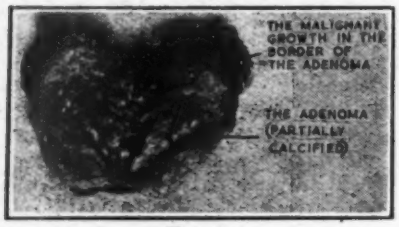

FIG. 4.

Case 3.—A woman aged 57 with no history of goitre. Interference by a thyroid tumour, with dyspnoea and increasing hoarseness of the voice, in the last two months. Physical examination showed great respiratory distress, and a large hard adherent left thyroid swelling with an extensive superficial venous network. Radiography revealed a cervico-mediastinal tumour with calcareous spots. At operation under local analgesia the subthyroid muscles were cut and a biopsy taken of the scirrhous growth. The right lobe was healthy. In spite of immediate *x*-ray therapy and tracheotomy the patient died after 10 days. At necropsy a large mass was found around the trachea like a ring, lying mostly in front of the trachea and behind the sternal manubrium; an old small calcified goitre was separable from the growth. Histologically the adenoma was medium-sized, with large follicles, and covered by an intact capsule. The cancer was trabecular at some points, anaplastic at others.

Case 4.—A woman aged 63 with no history of goitre. Pain in the right capsule for four months, and loss of weight for four years. A thyroid swelling appeared four months previously, medial, hard, and deep in the neck. Radiography showed a subcoracoid metastasis in the right scapular region. A total enlarged thyroidectomy was performed. *X*-ray treatment was impossible because of severe anaemia, and the patient died three months later. Pathological examination showed a hard white tumour containing three little pink encapsulated nodules the size of a cherry. Microscopically it was mostly anaplastic epithelium simulating sarcoma, in some places involving a goitre with very small and medium-sized follicles the fibrous walls of which had collapsed with the rush of neoplastic elements.

These four cases show clearly that carcinoma may arise around the capsule of an adenoma, which can be considered as a scar, and that even if the boundary is broken cancer grows from the outside but does not seem to arise in the adenoma.

B. Diffuse Goitre and Cancer

Case 5.—A woman aged 74 with a goitre for the past 22 years, painful and suddenly increasing in size in the last few weeks. A hard mass could be felt in the left lobe and be moved in the tissue planes. Total thyroidectomy was performed on the left, and subtotal on the right, which was healthy. Pathological examination showed two parts—the first an irregular-walled haematocele, the second a white and rather hard mass. Microscopically, adenomatous tissue with large and small follicles, with a flat epithelium and dense colloid, was seen in some parts and in others a trabecular epithelioma with considerable follicular differentiation and cylindro-cubic, rather regular eosinophilic cells. Capillaries were full of neoplastic nodules. Contiguity of these two areas was obvious and the border-line sinuous. The large follicle of a parenchymatous goitre lying in adenomatous and haemorrhagic tissue was quite different from any neoplastic structure, and at some points a malignant "feeler" pushed forward this border-line without invading it (Fig. 5). Degeneration of goitre into carcinoma was not seen anywhere.

FIG. 5.—The borderline between a diffuse colloid goitre and a trabeculo-follicular carcinoma.

C. Cancer Developing in Benign Tissue

Case 6.—This patient was operated on elsewhere and the specimen sent to our department. At one point trabeculo-follicular malignant structures were found surrounded by adenomatous tissue with inactive follicles. When looking closely at the so-called capsule of the malignant nodule we could clearly see a vascular lumen filled with a neoplastic thrombus and masses of erythrocytes. A well-defined endothelium was spread out all round the growth. Thus what seemed to be a carcinoma arising in the centre of an adenoma was in fact an embolus in the lumen of a vessel in the adenoma (Fig. 6).

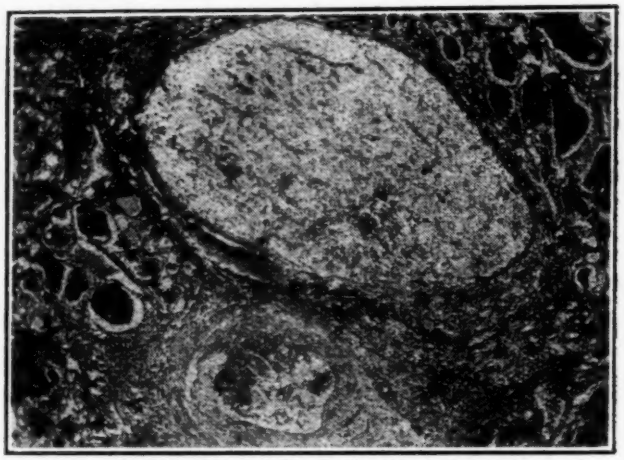

FIG. 6.—A malignant embolus in the vessel of an adenoma.

D. Adenoma as a New Growth in the Evolution of Cancer

Two cases lead us to suppose that an adenoma can form during or after the development of a cancer.

Case 7.—A man aged 39, with a very old goitre; he had had several crises of dyspnoea without any particular increase in its size. He had had paraplegia for two months. Examination showed a hard mobile tumour of the right lobe with a metastasis in the fourth thoracic vertebra. A right lobectomy with block dissection of the neck was performed and 4,500 r *x*-ray therapy given to the spine. One year afterwards a new growth appeared in the medial part of the neck, of the size of a small cherry, and a soft separable nodule connected with the left lobe was excised. Microscopical examination of a specimen from the first operation showed a polymorphic malignant lesion with follicles and trabeculae at some points, and here and there an anaplastic structure with isolated cells (Fig. 7). Sections of the so-called relapsed tumour (second operation) showed the small and medium-sized follicles of an adenoma in all parts, with

no sign of malignancy (Fig. 8). Death occurred five years later from the paraplegia, which had improved during the first two years. There was no recurrence in the thyroid area.

Case 8.—A woman aged 45, with a goitre for seven years previously; improved during the first four years with iodine, but got worse in the last two years, with a progressive increase in volume. Right extracapsular lobectomy and left subtotal thyroidectomy were performed. Four months later a small growth appeared on the right of the scar. A small, soft, separable growth was excised for biopsy and *x*-ray therapy was given. The first operative specimen showed trabeculae and follicles with an adenomatous stroma, and the second included two well-defined parts. The first part was a predominantly microfollicular epithelioma separated by a well-formed capsule from the second part, an adenoma with large follicles and flat epithelium and a big histiocytic reaction in the stroma.

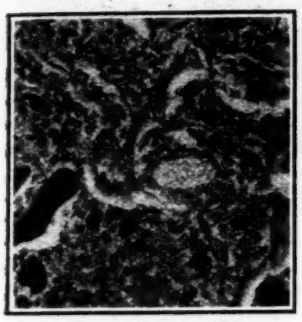

FIG. 7.—Trabeculo-vesicular epithelioma of the thyroid (Case 7).

These two cases show clearly that a benign process can appear concurrently with a malignant recurrence, or can occur by itself in the remaining healthy parenchyma after removal of the cancer. We have shown elsewhere that a benign thyroid growth may appear while another carcinoma arises in different parts of the body. In our view, and that of several workers, a thyroid hyperplasia may arise as a safeguard against malignancy. Perhaps the thyroid may show such a reaction to its own carcinoma. Both are quite independent anatomically. The high frequency of severe anaplastic forms after the age of 60—that is, when thyroid secretion has stopped—is another argument in favour of this hypothesis.

FIG. 8.—Histological structure of a so-called recurrence in the isthmus. (On several sections this pattern of benign adenoma was found repeated.) (Case 7.)

Discussion

It appears that a patient with a well-defined adenoma may go on to have a cancer. Two types of lesion may be noted: (1) the well-encapsulated adenoma which may be benign indefinitely alongside the cancer, as shown in some case reports above. (2) The improperly called "malignant adenoma," which is a carcinoma from the first. Careful examination of such nodules, even when macroscopically they appear to be separable, always shows a gap in the capsule at one point and an invasion of capillaries by a mass of thyroid tissue.

These facts, well emphasized by Graham, gave us reason to consider as malignant a thyroid adenoma of our group associated with a sacro-lumbar metastasis. While some sections showed an apparently benign tumour in some areas, a neoplastic embolus in the blood vessels emphasized malignancy in others (Fig. 9).

The term "adenomorphic carcinoma" seems suitable in general, and, in accord with recent work using radio-iodine, we also call it a malignant lobulating hyperplasia.

This discussion is not academic. Even if it is not always in conformity with the exact and true description of the early stages of cancer and benign goitre, reported data are numerous enough to lead to the following practical conclusions:

FIG. 9.—Malignant growth in a vessel of a so-called benign adenoma with bone metastases.

1. Use of antithyroid drugs such as thiouracil in a patient suffering from an apparently benign adenoma or toxic goitre may be dangerous, as it may turn a hyperplastic parenchyma to malignancy.

2. Enucleation of a so-called adenoma, even if apparently well isolated, does not prevent the appearance of carcinoma, because the malignant process can develop in the surrounding tissue, or because, the adenoma being already cancerous, the operation was obviously an unsatisfactory treatment.

Summary

The view that thyroid carcinoma may arise in a pre-existing adenoma is challenged.

Evidence from the relative incidence of adenoma and cancer in the two sexes and at different ages is against it. It is suggested that any adenoma which seems to turn malignant in less than ten years from its initial appearance was in reality malignant from the first.

Histological sections are presented to show that adenoma and carcinoma may coexist, and that adenoma may follow cancer, which can also develop in a diffuse goitre or from normal tissue.

The significance of these observations for practical therapy is discussed.

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EFFECT OF CORTISONE UPON SKIN SENSITIVITY TO TUBERCULIN IN SARCOIDOSIS

BY

D. A. PYKE, M.B., M.R.C.P.

AND

J. G. SCADDING, M.D., F.R.C.P.

(From the Department of Medicine, Postgraduate Medical School of London, W.12, and the Institute of Diseases of the Chest, Brompton)

The observations reported in this paper were started when, in a patient suffering from sarcoidosis and receiving cortisone, a change in the skin sensitivity to tuberculin was noticed. This patient showed a diffuse nodular infiltration of the lungs, histological changes typical of sarcoidosis on biopsy of the liver, and a persistently negative Mantoux reaction, no reaction having been evident at any time after the intradermal injection of 100 T.U.* of old tuberculin (O.T.) on several occasions during the preceding six months. Cortisone was administered intramuscularly in a dose of 100 mg. daily. Forty-eight hours before this treatment was started 100 T.U. of O.T. had been injected intradermally, and had produced no reaction when read at the usual interval of 48 hours. On the fourth day of cortisone administration a small flare was noted at the site of this tuberculin injection. On the fifth day this had developed into an indurated area 25 by 17 mm., which gradually faded within the next two days. Also on the fifth day, another intradermal injection of 100 T.U. of O.T. was made; this produced an indurated area 20 by 25 mm. on the sixth day, which was still present but fading on the seventh day, and did not disappear completely until the eleventh day. On the sixth day 10 T.U. of O.T. was injected. After 24 hours there was a small flare, and at 48 hours an area of induration 10 by 8 mm., which gradually faded over the next two days. On the eighteenth day 100 T.U. of O.T. was injected, but produced no reaction. These reactions resembled normal positive tuberculin reactions, but appeared rather earlier and faded rather more quickly. This experience led us to investigate the effect of cortisone on the skin sensitivity to tuberculin in patients with sarcoidosis.

Clinical Data

We have made observations on 14 patients who showed a clinical picture compatible with sarcoidosis—13 with lung changes and the remaining one with gross hilar lymph-node enlargement; in all of them histological confirmation had been obtained, sarcoid-type tubercles in an active phase having been found in biopsy material. This was obtained from the liver in six cases, from lymph nodes in four, from skin in three, and from a nodule in the breast in one. Although a negative tuberculin reaction was not included in the criteria for diagnosis, it was in fact found in most of the cases investigated. Eleven of the 14 showed no reaction to at least 100 (usually 1,000) T.U. of O.T. or to 250 T.U. of purified protein derivative (P.P.D.); two reacted to 10 T.U. and one to 100 T.U. of O.T.

*Throughout this paper quantities of tuberculin will be stated in terms of tuberculin units (T.U.). 1 T.U. ≡ 0.00002 mg. P.P.D. ≡ 0.1 ml. of 1:10,000 O.T.

Effect of Cortisone Administered Intramuscularly

Cortisone was administered intramuscularly to 10 patients who were Mantoux-negative to at least 100 T.U. The cortisone was given in a single daily intramuscular injection of 100 mg. for 20 days. A dose of tuberculin of the type used for the preliminary Mantoux tests, and equal to or less than that used in these tests, was injected intradermally at intervals during the course of this treatment. The size of any resulting area of induration or erythema was measured at 24 and 48 hours. Some change in skin reactivity to tuberculin was observed at some stage in 8 of the 10 patients.

In six of these (including the patient already described) the reaction was similar in appearance to a normal positive Mantoux reaction. The time at which the change in skin reactivity was first observed varied from case to case. The earliest tuberculin injections to which reaction was detected were made on the third, fifth, fifth, sixth, tenth, and seventeenth days respectively. In one patient skin sensitivity was still present on the nineteenth day, in three it had disappeared by the eighteenth day, and in two no further observations were made. The reactions were accelerated as compared with the normal positive tuberculin reaction. They all reached a maximum by 24 hours, except one which was at its greatest 48 hours after the injection. Although the reactions faded quickly, and had usually disappeared in 72 hours, all these patients had at least one reaction which was still showing an area of induration at 48 hours. Usually the later tests became less intense and faded more quickly.

In two patients the observed skin reaction to tuberculin consisted only of the appearance of erythema, without induration. This constituted a definite change, since there had been no reaction of any sort before cortisone administration. The erythema reached its maximum of 20–30 mm. in diameter by 24 hours after the tuberculin injection, and faded rapidly. In both cases the greatest reaction was observed to an injection made soon after the beginning of cortisone administration. It could not be obtained again on the tenth day or later in one case, and on the thirteenth day or later in the other.

In only two patients was no change in skin reactivity to tuberculin observed at any time during cortisone administration.

Two of the patients who had shown a response early in a course of cortisone administered intramuscularly, and in whom the induced skin reactivity to tuberculin had disappeared later in the course, received courses of cortisone 100 mg. daily by mouth after an interval. In one no reaction to intradermal tuberculin was observed at any time during oral administration of cortisone, started eight weeks after the last intramuscular injection. The other had shown a response to 100 T.U. of O.T. early in the course of intramuscular cortisone, although she normally failed to react to 1,000 T.U. During the oral administration of cortisone, started six weeks after the last intramuscular injection, she showed a wheal 20 mm. in diameter 24 hours after the injection of 1,000 T.U. of O.T. on the fifth and sixth days, a much smaller reaction on the twelfth day, and none on the fifteenth; 100 T.U. produced only erythema 24 hours after injection on the fifth day, but there was no response to this dose of tuberculin later.

Effect of Local Cortisone

In 12 of the 14 cases the effect of cortisone mixed with the tuberculin used for intradermal injection was studied, whenever possible before intramuscular cortisone had been given. The technique used was similar to that of Vollmer (1951). At least three injections were made in each case: a dose of tuberculin equal to that which had previously been used for the determination of tuberculin sensitivity; the same dose of tuberculin with 1.25 mg. of cortisone; and 1.25 mg. of cortisone alone (1.25 mg. of cortisone is contained in 0.05 ml. of the standard suspension). The test

solutions were each made up to a total volume of 0.1 ml. for intradermal injection by adding to 0.05 ml. cortisone suspension 0.05 ml. of tuberculin solution of twice the test strength to make the cortisone–tuberculin injection, and 0.05 ml. of saline solution for the cortisone injection. In four cases a further control, consisting of 0.05 ml. of the aqueous vehicle in which cortisone is suspended diluted to 0.1 ml. with normal saline, was used, but produced no reaction. In a few subjects, not in this series and not suffering from sarcoidosis, we have found a skin reaction to the aqueous vehicle, but this was invariably inhibited by cortisone, and therefore cannot be a confusing factor.

Nine of the 12 patients in whom the effect of local cortisone was tested were normally Mantoux-negative. Seven of these showed changes similar to those obtained with systemic cortisone. Areas of induration with surrounding erythema appeared at the site of the mixed tuberculin and cortisone injection, usually reaching a maximum between 24 and 48 hours, and then fading. At the site of the tuberculin injection there was no reaction. At the site of the cortisone injection a small intradermal nodule, presumably due to the particulate nature of the cortisone suspension, was often observed. This was quite different from the induration of a tuberculin reaction, and had no surrounding erythema.

In the three patients who were Mantoux-positive to 100 T.U. or less the effect of the addition of cortisone to the injection was to inhibit the reaction which was evident at the site of injection of tuberculin alone.

Correlation between Results of Systemic and of Local Administration of Cortisone

Eight out of the 11 Mantoux-negative patients were investigated with both systemic and local administration —five showed an altered response after both methods, two showed a response with local administration only, and one with systemic only. In two cortisone was given by intramuscular injection only, and one of these showed a definite response and one erythema. One patient was tested with local cortisone only, and showed no response. The results are summarized in the Table.

Summary of Effects of Cortisone on Skin Sensitivity to Tuberculin in 14 Patients with Sarcoidosis

Case	Sex	Age (Years)	Original Skin-sensitivity to 100 T.U.	Route of Administration: Intramuscular (100 mg. daily) — Response	Intramuscular (100 mg. daily) — Day of Cortisone Course on which Tuberculin Injection Causing Greatest Reaction was Given	Local (1·25 mg. with Tuberculin)
1	F	43	Negative	+	6	+
2	F	32	,,	0	—	+
3	M	34	,,	+	6	+
4	F	27	,,	+	10	0
5	F	43	,,	0	—	+
6	F	31	,,	+	7	Not tested
7	M	43	,,	±	1	,, + ,,
8	F	23	,,	±	5	+
9	F	51	,,	+	5	+
10	M	33	,,	+	17	+
11	F	27	,,	Not given		0
12	F	34	Positive	,, ,,		Inhibited
13	F	28	,,	,, ,,		,,
14	F	27	,,	,, ,,		,,

+ = skin reaction persisting 48 hours in subject normally insensitive to tuberculin.
± = skin reaction persisting 24 hours, but less than 48 hours.
Inhibited = skin reaction to tuberculin inhibited.

Cases Excluded from Analysis

In addition to the 14 patients already described, three patients with proved sarcoidosis have been tested—two with both systemic and local administration of cortisone, and one with local only. For what were considered to be good reasons these cases have been excluded from the analysis presented above. In one case the diagnosis was proved histologically more than three years ago; the histological changes then were those of an inactive phase, and the residual changes now consist only of probably non-specific residual fibrosis and emphysema in the lungs. The other two presented the complicating factor of having completed a prolonged course of systemic cortisone shortly before the tests were made. All the tests on these three cases were negative.

Discussion

The absence of skin sensitivity to tuberculin which is found in many cases of sarcoidosis is one of the most remarkable features of this syndrome, and has been investigated extensively. It is different in important respects from the lack of sensitivity shown by normal persons who have not been infected with tuberculosis. The reported inability to cause conversion of the negative Mantoux reactions in some cases of sarcoidosis to positive by B.C.G. vaccination (Lemming, 1940; Israel *et al.*, 1950) and the presence of a tuberculin-neutralizing factor ("anticutin") in the sera of some patients with sarcoidosis (Martenstein and Jadassohn, 1923; Wells and Wylie, 1949; Sterling, 1950) are indications of this difference. Neither of these phenomena is constantly found; but each of them has been reported in enough cases to support the view that the negative Mantoux reaction in sarcoidosis may well be more than an indication of the simple absence of tuberculous infection. The phenomenon reported in this paper is likewise inconstant, but it also indicates something peculiar about the negative Mantoux reaction in sarcoidosis. Observations on two patients have failed to show any correlation between the presence of tuberculin-neutralizing factor and the induction of temporary tuberculin sensitivity by cortisone. Specimens of serum from these two patients, in both of whom temporary skin sensitivity to tuberculin was induced by cortisone administered both systemically and locally, were tested by the method of Wells and Wylie. No tuberculin-neutralizing effect was found in sera taken before cortisone treatment or during the phase of tuberculin sensitivity.

In the few healthy Mantoux-negative individuals in whom we have tried the effect of cortisone added to the tuberculin injected for a tuberculin test no modification of the negative test has been observed.

The positive Mantoux reaction found in healthy persons who have had a tuberculous infection, or in sufferers from tuberculosis, is usually inhibited or diminished by cortisone, administered either systemically or locally (Long and Favour, 1950; Le Maistre *et al.*, 1951; Vollmer, 1951; Wallner *et al.*, 1952); we have confirmed this observation and, as recorded above, have found it also to hold true in three patients with the clinical and histological picture of sarcoidosis in whom the Mantoux reaction was positive. The only authors to report enhancement of tuberculin skin sensitivity by cortisone are Coste *et al.* (1951). In some patients under treatment by cortisone or A.C.T.H. for a variety of non-tuberculous diseases but with positive Mantoux reactions they found a slight increase in the size of the reaction, together with acceleration of its appearance. This increase was inconstant and usually of slight degree, and was greatest after prolonged treatment (one month).

In general, cutaneous hypersensitivity of the "tuberculin" type appears to be inhibited, diminished, or unaffected by cortisone; the skin sensitivity to tuberculin induced by systemically or locally administered cortisone in subjects previously insensitive which we have observed in some cases of sarcoidosis appears to be unique. This phenomenon is obviously of the greatest theoretical interest in relation to the aetiology of sarcoidosis, and may prove to be of some practical importance as a diagnostic test; but our present purpose is no more than to record its occurrence.

Summary

The effect of cortisone upon skin sensitivity to tuberculin was investigated in 14 patients with sarcoidosis.

Ten patients who normally failed to react to at least 100 T.U. of tuberculin intradermally received 100 mg.

of cortisone daily by intramuscular injection. In eight of these skin sensitivity to tuberculin was detected at intervals ranging from 6 to 17 days after the first injection of cortisone; in six the reaction produced by tuberculin during the period of sensitivity persisted, with induration, up to 48 hours, and in two it consisted of erythema, evident at 24 hours but fading at 48 hours. In those patients tested repeatedly this sensitivity was transient, even though the cortisone was continued.

In nine patients normally not reacting to at least 100 T.U., intradermal injection of 1.25 mg. cortisone with a dose of tuberculin equal to the greatest to which the patient had previously failed to respond produced a reaction with induration and erythema persisting at least 48 hours in seven, and no response in two.

In three patients normally sensitive to 100 T.U. or less, similar local administration of cortisone with tuberculin inhibited the reaction produced by tuberculin alone.

We are grateful to the house-physicians at Brompton Hospital and Hammersmith Hospital for their co-operation in these observations. Part of the cortisone used was supplied by the Medical Research Council.

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TESTING OF SKIN DISINFECTANTS

BY

PETER STORY, M.D.

(From the Department of Pathology, St. Bartholomew's Hospital)

Skin disinfectants may be compared by their killing effect on normal skin flora or bacteria applied to the skin, and numerous techniques are based on this idea. Pathogenic bacteria are nearly always transient on the skin surface, where they can be killed by suitable chemicals, although in special circumstances pathogens such as *Staph. pyogenes* become established as part of the resident flora in deeper layers of the skin, where they may not be reached by disinfectants (Price, 1938). Normally there are resident bacteria deep in the skin which are mainly inaccessible to disinfectants or bacteriological sampling, but they are non-pathogenic organisms of little or no practical importance. Lovell (1945) has ingeniously demonstrated these deeply situated bacteria by sectioning and staining excised skin after a period of incubation in a moist chamber to allow organisms to multiply and become visible histologically.

Although there is general agreement that skin cannot be chemically sterilized throughout its thickness without destroying it, Gardner and Seddon (1946) have shown that the skin cocci can sometimes be eliminated completely. They excised and cultivated pieces of normal skin at the beginning and end of surgical operations; after preliminary treatment with 2% aqueous iodine 58% yielded no growth of skin cocci; corresponding results with 5% and 1% aqueous cetrimide were 34% and 25%.

This last method could not be applied safely to skin contaminated with known pathogens, and to test a disinfectant's action against such organisms a practical method is to apply bacteria to the skin followed by disinfectant and recovery of any surviving bacteria after varying periods. This does at least supply the information that a disinfectant will destroy pathogenic bacteria known to be on the skin surface, where, indeed, they are most likely to be found under normal circumstances. Although open to the objection that bacteria placed on the skin may not be affected by disinfectants in the same way as natural transient flora, it is probably the best method of testing available.

In the investigation reported here this technique was used to test the efficacy of several skin disinfectants against strains of *Staph. pyogenes, Bact. coli, Ps. pyocyanea,* and *Proteus vulgaris* isolated from wound swabs. These organisms were all penicillin-resistant, and penicillin was added to the culture medium to suppress growth of normal skin flora. Most of the tests were carried out against a strain of *Staph. pyogenes* which grew freely in the presence of 0.5 unit of penicillin per ml. In experiments on quaternary ammonium compounds, such as cetrimide, the recovered organisms were mixed with sterile milk before cultivation, since it has been shown (McCulloch, 1947) that this substance will neutralize the bacteriostatic action of cetrimide. Bacteria were recovered from the skin by a method similar to Burtenshaw's (1938).

Numerous techniques have been employed in recovering bacteria from skin surfaces; they include rubbing the skin with a moist swab and then agitating the swab in broth and making pour plates (Colebrook, 1930) or streaking out the swab on an agar plate (Gardner and Seddon, 1946). Price (1938) devised the method of washing the hands and forearms in a series of bowls of water and cultivating this water; he has recently described a method for repeated bacteriological sampling of a small skin area which he calls "spot testing" (Price, 1951). Burtenshaw (1938) applied a rectangular glass chamber to the skin, added saline, and scraped the skin with a glass slide to make a suspension of organisms from which he made viable counts. Brown *et al.* (1944) filled watch-glasses to the brim with agar and placed them on skin to collect the bacteria. Most elaborate, perhaps, is the method of Nungester and Kempf (1942), who rubbed a mouse's tail with pneumococcal culture, dipped the tail into disinfectant for two minutes, and then cut off ½ in. (1.3 cm.) and placed it in the mouse's peritoneal cavity. Any pneumococci surviving exposure to the disinfectant caused a fatal peritonitis.

Methods

For each disinfectant test six circular areas 4 cm. in diameter were outlined on the forearm or thigh, using a glass ring and skin pencil. Most tests were done on the forearm, the skin being unwashed. The bacterial inoculum to each test area consisted of 1 drop, from a pipette delivering 40 drops/ml., of a 1/10 dilution of 20-hour broth culture (in the case of *Ps. pyocyanea* only a 1/100 dilution was used). Each drop was spread over its circular area with a wire.

Bacteria were added to the first five circular areas. When dry the first four circles and the last (containing no added bacteria) were treated with disinfectant applied with a cotton-

wool-tipped throat swab in as uniform a manner as possible, fairly freely, but not enough to run. A stop-watch was started at the first application of disinfectant and areas were sampled as described after half, one, two, and five minutes. The fifth area, carrying added bacteria but no disinfectant, was then sampled; it served as a control against autogenous disinfection, and several dilutions were made so as to obtain a total count. The sixth and last circle contained disinfectant but no added bacteria; it acted as a carry-over control and was sampled in the same way as the other areas, and 1 ml. was added to a pour plate which was then inoculated with the test organism. This showed whether an inhibitory concentration of disinfectant was being carried over into the culture medium during sampling from the test areas.

In those experiments in which Gram-negative bacilli were used as test bacteria they were exposed to disinfectant for a half and two minutes only (Tables I and II).

TABLE I.—*Detailed Results of Two Tests Against Staph. pyogenes Giving Numbers of Organisms Recovered from Each Test Area and Controls*

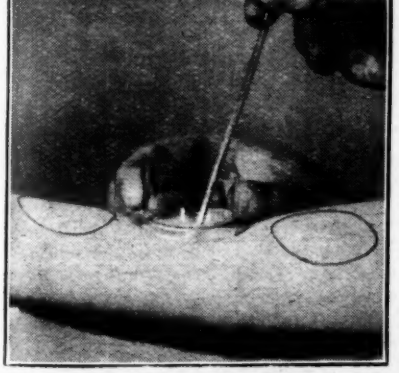
Disinfectant	Test Areas (1/10)					Control Area		Carry-over Control
	½ min.	1 min.	2 min.	2 min.*	5 min.	1/200	1/2,000	
1% cetrimide in 70% spirit	0	0	0	0	0	380	40	Satisfactory
1/1,000 zephiran in 50% alcohol ..	40	8	1	0	0	120	—	,,

* Culture containing no milk.

TABLE II.—*Detailed Results of Two Tests Carried Out Against Ps. pyocyanea Giving Numbers of Organisms Recovered from Each Test Area and Controls*

Disinfectant	Test Areas (1/10)		Control Area		Carry-over Control
	½ min.	2 min.	1/50	1/500	
1% iodine in 70% spirit	0	0	+	136	Satisfactory
1% aqueous cetrimide	160	48	+	160	,,

Bacteria were recovered from the skin by means of glass rings 4 cm. in diameter, 2.5 cm. deep, and 1.5 mm. thick. One of these rings was placed over a test area, held in position by the subject, and 5 ml. of sterile distilled water was added; the operator quickly and systematically rubbed the skin for 15 seconds, using a glass spreader with an arm 1.5 cm. long (see Fig.), and then took a 1-ml. sample of fluid. The aim was to get bacteria on the skin surface into uniform suspension in the water. Viable counts were made by a pour-plate method after 48 hours' incubation at 37° C. Using this technique, we got a higher recovery of bacteria from adjacent areas of normal skin and of bacteria placed on the skin than we did by either of the swabbing methods.



Glass ring held on skin contains water and glass spreader. Note the adjacent test areas outlined by skin pencil.

In all experiments on quaternary ammonium compounds 1 ml. of fluid from the glass ring was added to 1 ml. of sterile milk, mixed, and 1 ml. of the mixture was used for a pour plate or further dilutions (necessary in the control) which were made in distilled water. In the same way 1 ml. of milk was added to the fluid from the carry-over control. When iodine was being tested enough sodium thiosulphate was placed in the Petri dishes to neutralize any iodine carried over.

Pour plates were made by placing in a Petri dish 0.5 ml. of penicillin solution (10 units/ml.), 1 ml. of fluid from the glass ring, and about 14 ml. of agar melted and cooled to 48° C.; the final concentration of penicillin was thus 0.3 unit/ml. The normal flora from the forearms of several individuals was sampled, 1 ml. of fluid from each glass ring being added to melted agar containing 0.3 unit of penicillin per ml. and 1 ml. into agar with no penicillin; altogether 36 skin areas were examined in this way. In the absence of penicillin an average of 231 colonies per 1/5 test area was obtained, in contrast to 8 when penicillin was present. Usually with the antibiotic there were 0 to 3 colonies, but one subject carried very large numbers of penicillin-resistant organisms, which raised the average.

McCulloch (1947) has shown that the bacteriostatic action of cetrimide on *Staph. aureus* is neutralized by skim milk. In preliminary experiments with the strain of *Staph. pyogenes* used in these tests 10% skim milk and 10% human plasma were about equally effective in this respect for cetrimide and also for "bradosol," "zephiran," and dynium chloride. In order to demonstrate this antibacteriostatic action of milk during skin experiments a second 1-ml. sample was taken after the 2-minute test, diluted with 1 ml. of water instead of milk, and made into a pour plate; counts were consistently higher in the milk-containing plates.

Recovery of bacteria from control areas was always satisfactory with Gram-negative organisms. On a few occasions recovery of *Staph. pyogenes* was poor; this did not occur intermittently but in small batches of tests towards the end of the investigation. These tests were considered to be invalid. Several subsidiary experiments failed to show a cause for this.

At the end of an experiment skin which had been contaminated with bacteria was treated with 1% iodine in spirit and subsequently washed well with soap and water. This precaution is, of course, essential when working with a test organism such as a penicillin-resistant strain of *Staph. pyogenes*. After an experiment a skin area was not used again until at least two to three days had passed.

Results

The result of a disinfectant test was regarded as satisfactory when not more than one colony grew on the pour plates; this represented not more than 5–10 surviving bacteria in a test area. At least 10.000 organisms were recovered from each staphylococcal control area, and often 50.000–100.000; recoveries of Gram-negative bacilli were generally higher. This is in line with Gardner's (1948) conception of "virtual disinfection" involving the death of at least 99.9% of bacteria on the skin surface.

Of the disinfectants tested against *Staph. pyogenes* the following were found effective within 30 seconds: 1% iodine, 1% and 10% cetrimide, or 1/1,000 dynium chloride in 70% industrial spirit (74 O.P.). In all these tests there were no surviving bacteria. Seventy per cent. industrial spirit alone was effective in 30 seconds: a few of the plates grew one colony; after two minutes all plates were sterile. Four per cent. aqueous cetrimide was not completely effective in 30 seconds, but was after two minutes. With 10% cetrimide carry-over controls were unsatisfactory, showing either no growth or considerable inhibition.

Other disinfectants tested which were not consistently effective even after five minutes included 1% and 2% aqueous cetrimide, 1% aqueous bradosol, and 1/1.000 zephiran in 50% alcohol. Only a few tests were carried out with the last two substances.

Bact. coli, *Ps. pyocyanea*, and *Proteus vulgaris* behaved alike against the disinfectants tested. Completely effective within

30 seconds were 1% iodine or 1% cetrimide in 70% spirit or 70% industrial spirit alone. One per cent. aqueous iodine was effective against *Ps. pyocyanea* in 30 seconds; no other organisms were tested with this disinfectant. One per cent. aqueous cetrimide was ineffective against all the Gram-negative bacilli; after two minutes' exposure to disinfectant there were large numbers of surviving bacteria. No tests on Gram-negative bacteria were carried beyond two minutes.

A total of 157 tests were made by the method described here; Table III gives the numbers of experiments for each disinfectant and test organism, with the proportion yielding "virtual disinfection."

Discussion

It will be seen from Table III that, in the case of some disinfectants, the numbers of tests do not permit any firm conclusions to be drawn; generally, however, results agree with those of other workers using different methods.

TABLE III.—*Proportion of Tests Resulting in "Virtual Disinfection"*

Disinfectant	*Staph. pyogenes*				*Ps. pyocyanea*		*Bact. coli*		*P. vulgaris*	
	½ min.	1 min.	2 min.	5 min.	½ min.	2 min.	½ min.	2 min.	½ min.	2 min.
1% iodine in 70% spirit	15/15	15/15	15/15	15/15	16/16	16/16	5/5	5/5	5/5	5/5
1% aqueous iodine	—	—	—	—	5/5	5/5	—	—	—	—
1% aqueous cetrimide	6/9	6/9	6/9	6/9	0/5	1/5	0/5	0/5	0/5	0/5
2% aqueous cetrimide	3/5	3/5	3/5	3/4	—	—	—	—	—	—
4% aqueous cetrimide	4/5	4/5	5/5	5/5	—	—	—	—	—	—
1% cetrimide in 70% spirit	10/10	10/10	10/10	10/10	5/5	5/5	5/5	5/5	5/5	5/5
10% cetrimide in 70% spirit*	10/10	10/10	10/10	10/10	—	—	—	—	—	—
1% aqueous bradosol	1/6	0/6	2/6	5/6	—	—	—	—	—	—
1/1,000 zephiran in 50% alcohol	3/6	2/6	3/6	4/6	—	—	—	—	—	—
1/1,000 dynium chloride in 70% spirit	5/5	5/5	5/5	5/5	—	—	—	—	—	—
70% industrial spirit	10/10	10/10	10/10	10/10	5/5	5/5	5/5	5/5	5/5	5/5

Denominator represents total number of tests with adequate controls.
* Carry-over control unsatisfactory.

In these experiments 70% industrial spirit (74 O.P.) alone produced "virtual disinfection" within 30 seconds with the four test organisms. This is a more rapid disinfectant action on skin than has generally been attributed to 70% alcohol; Gardner (1948), for example, found that it required two minutes to kill organisms on the skin surface. It may be that a more liberal application of disinfectant was made to test areas in this investigation. However, as described above, care was taken not to add an excess which would run on the skin, and certainly less was applied than would normally be put on the skin before a surgical incision.

As was to be expected, 70% spirit containing other disinfectants such as 1% cetrimide or 1/1,000 dynium chloride also produced "virtual disinfection" of skin areas within 30 seconds. The performance of 70% spirit alone in these experiments was so good that it is difficult to decide whether the addition of other disinfectants improves it. On testing 1% cetrimide in 70% spirit and 70% spirit against the Gram-negative bacteria both produced completely sterile test areas after 30 seconds. When *Staph. pyogenes* was tested 5 to 10 organisms (which is "virtual disinfection") survived on four of the areas exposed to 70% spirit for 30 seconds, whereas all plates from areas treated with 1% cetrimide in spirit were sterile. As only 10 tests were done with each of these disinfectants against *Staph. pyogenes* this cannot be regarded as significant, but if similar results were repeated it would suggest that 1% cetrimide in spirit is a somewhat better skin disinfectant than 70% spirit alone.

Gardner (1948) found that 10% cetrimide in 70% alcohol killed *Ps. pyocyanea* on the skin in 30–45 seconds. When this disinfectant was tested against *Staph. pyogenes* by the technique described here an inhibitory concentration of cetrimide was carried over on sampling into the cultures (even when milk was added) so that they were inevitably sterile.

In 29 experiments 1% and 2% aqueous cetrimide were not completely effective within two minutes against any of the test organisms, but they performed best against *Staph. pyogenes*. Gardner and Seddon (1946) found that even 5% aqueous cetrimide did not produce "virtual disinfection" of *Ps. pyocanea* in one and a half minutes.

Some importance is attached to neutralization of the bacteriostatic action of cetrimide. This has not been done in other investigations, though controls have usually been designed to demonstrate carry-over of an inhibitory concentration of disinfectant which does not serve the same purpose. Failure to prevent bacteriostasis might make a disinfectant appear more effective than it is if some surviving organisms were unable to grow into visible colonies. As milk and human plasma are almost equally effective in reversing the bacteriostatic effect of cetrimide and some other quaternary ammonium compounds it seems possible that, in a wound, any organisms exposed to but not killed outright by cetrimide could be revived by the plasma which is present.

In common with numerous other investigations, iodine in spirit was found consistently effective. Forty-one tests were carried out with 1% iodine in 70% industrial spirit against the four test organisms, and after 30 seconds' exposure there were no survivors.

Summary

A method of testing skin disinfectants is described which includes: (1) using penicillin-resistant test organisms with penicillin in culture medium to suppress natural skin flora; (2) counteraction of the bacteriostatic effect of quaternary ammonium compounds with sterile skim milk; and (3) recovery of skin bacteria by use of a glass ring

Several disinfectants have been compared by their ability to kill *Staph. pyogenes, Bact. coli, Ps. pyocyanea*, and *Proteus vulgaris* on the skin.

One per cent. iodine or 1% cetrimide in 70% industrial spirit (74 O.P.) killed all test organisms within 30 seconds, and 70% spirit alone produced "virtual disinfection" within that time. Ten per cent. cetrimide or 1/1,000 dynium chloride in 70% spirit and 1% aqueous iodine were effective within 30 seconds against the bacteria tested; some other disinfectants were only partially effective.

I am indebted to Professor L. P. Garrod for suggesting this investigation and for advice during its progress. Miss M. Rhodes gave me valuable technical assistance and carried out many of the tests.

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A medical gastronome, Dr. Paul Ramain, from Douvaine, in Savoy, has won a prize of 100,000 francs for the best book of the year on food (*The Times*, November 14). His book, which is not yet published, describes 336 new ways of cooking and serving edible fungi. The prize was awarded by a jury of members of the Club des Cent, a gourmets' association. Dr Ramain is clearly a man of parts: his name is also associated with a small Alpine butterfly which he classified.

THE PROTEIN CONTENT OF THE BREAST MILK OF AFRICAN WOMEN

BY

D. B. JELLIFFE, M.D., M.R.C.P., D.C.H. D.T.M.&H.

(From University College of the West Indies, Jamaica; lately of the Department of Medicine, University College, Ibadan, Nigeria)

Infant-feeding follows a similar pattern in most tropical African countries. Cow's milk is rarely available, and breast-feeding is therefore the rule. This is usually begun during the first few days of life and continued for two to three years, although occasional feeds may be given as late as six years. Supplementary feeding consists almost entirely of carbohydrate gruels and pastes, including plantains, maize, cassava, and bananas. These may be given in the early months of infancy, but more usually are introduced at about the age of 6 months (Housden, 1950; Brock and Autret, 1952; Jelliffe, 1952a). When weaned completely, children share the adult diet, and although this food is slightly more nutritious it still consists almost exclusively of carbohydrate. It must be stressed that all forms of artificial feeding with dried cow's milk, etc., are prohibitively expensive for the vast majority of African mothers.

As is well known, the syndrome of malignant malnutrition, or kwashiorkor, occurs most commonly some months after the child has been weaned from the breast, and is probably produced by the gross and cumulative lack of protein in the diet. However, occasional cases are seen while the child is being breast-fed, usually after the age of 1 year, and very rarely much earlier in infancy. Thus, Gelfand (1951) has reported a case of kwashiorkor from Southern Rhodesia in an African baby of 3 months.

In Ibadan and in many parts of Africa pregnant women and nursing mothers do not seem to receive special food, and their diet is certainly very deficient in protein, as has been emphasized recently by Woodruff (1951). In view of the prolonged lactation in these poorly nourished women, it was thought likely that the protein content of their breast milk might have deteriorated during the later stages of breast-feeding, and the following investigation was accordingly undertaken.

Collection and Analysis of Specimens.—Specimens of breast milk (5–10 ml.) were collected from 88 consecutive apparently healthy Yoruba nursing mothers in Ibadan. All were of a low-income group and most of them were poorly nourished. The length of lactation varied from 1 to 36 months. The milk was sealed to prevent evaporation, after the addition of 0.1 g. of boric acid and 1 minim (0.06 ml.) of commercial formalin as preservatives, and was shipped to the Mead Johnson Research Laboratories. For most of the journey the specimens were refrigerated. On arrival 12 samples were found to be broken or clotted. These were discarded, leaving 76 in good condition, which were analysed for total nitrogen, using the semi-micro-Kjeldahl method.

Results

The protein content was calculated from the figures for total nitrogen (N × 6.38). The mean for the group was found to be 1.04%, with a range of from 0.59% to 1.76%.

Discussion

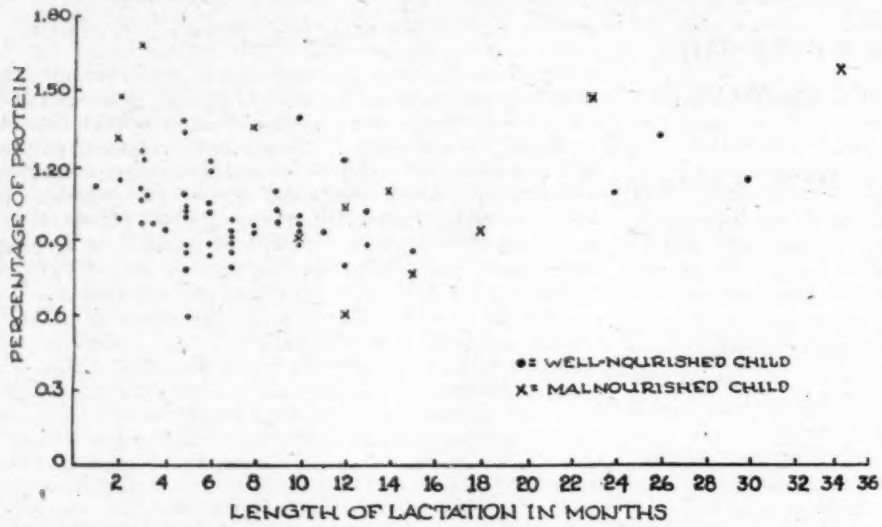
The protein content of human breast milk, as shown by analyses in Caucasian women, varies with different stages of lactation. During the first days of secretion the colostrum produced contains 4–8%. This rapidly decreases during the first two weeks and then remains constant for about a month and a half. About two months after the beginning of lactation, and subsequently, a very gradual decline in the protein probably occurs. It must be noted, however, that few estimations seem to have been made late in lactation—that is, over 10 months—in Caucasian women.

"Mature" human milk—after the first month of lactation—usually shows a protein content of 1–2%. Various investigators have recorded the following results: Holt *et al.* (1915), 1.15%; Schlossmann (1902), 1.25%; Bell (1928), 1.21% (at 7–8 weeks); Nims *et al.* (1932), from 0.98% to 1.96%, etc. More recently, in an extensive investigation of 200 healthy American women, Macy (1949) reported the surprisingly low mean figure of 1.06% (range 0.73% to 2%) in mature milk. Clements (1949), quoting unpublished data, also notes that the protein content of breast milk of healthy Australian women, as shown by analyses made at the Australian Institute of Anatomy, Canberra, is lower than the usually quoted textbook figures. Not many figures are available for milk taken very late in lactation. In America, Holt and his associates (1915) found an average of 1.07% protein in 10 nursing mothers who had been lactating for from 10 to 20 months. More recently, in 1941–2, Kon and Mawson (1950), in the course of a large-scale investigation into the composition of breast milk in Reading under wartime dietetic conditions, found the protein content to be 1.17% in 33 women between the 21st and 24th weeks of lactation, while in 10 mothers still lactating at from 25 to 28 weeks this had fallen to 1.00%. In 1946–7, Gunther and Stanier (1951) analysed the breast milk of mainly undernourished German mothers in Wuppertal and, in 11 women between the 9th and 28th weeks of lactation, found the protein content to be 1.17%.

Few analyses seem to have been undertaken in the Tropics, especially in Africa, and these have shown an unexpectedly high protein content to occur in malnourished mothers all over the world. Bray (1928) found the protein content to be 1.06% in Nauru, in the Pacific, while Bunce (1931) analysed the breast milk of Burmese and Indian mothers in Rangoon and reported the protein to be within normal Caucasian limits. In Africa, Dufour and Gourry (1934) have investigated the milk of women at Dakar; this was found to contain 1.24% protein. In the case of kwashiorkor in a 3-months-old breast-fed baby reported from Southern Rhodesia by Gelfand (1951) the mother's milk contained 1.35% protein. Recently Walker *et al.* (1952) have given a preliminary outline of an investigation of the breast milk of 200 urban Bantu women undertaken at the Nutrition Unit of the South African Institute of Medical Research at Johannesburg. They found the usual wide range of variation, but the average content of protein, as well as of other constituents, was almost identical to that given for Caucasian mothers.

In the present series of 76 specimens of breast milk obtained from African nursing mothers in Ibadan, the mean protein content was found to be 1.04%. In view of the protein-deficient diet of these women and the extreme length of lactation, it is felt that this figure is gratifyingly high. In particular, there was no apparent diminution of the protein content with prolonged lactation. This lack of relationship is emphasized by the "scatter diagram." For example, a woman who had been suckling her child for 36 months showed 1.56%, while a grandmother who had been breast-feeding her grandchild for three months was found to have 1.68%. In addition, again as shown by the "scatter diagram," there appeared to be no obvious relationship between the protein content and the nutritional status of the child.

Growth curves of African infants usually show a satisfactory gain in weight for the first six months or so, when



"Scatter-diagram" showing the lack of relationship between the protein content of the specimens of breast-milk and (*a*) the length of lactation and (*b*) the nutritional status of the infants.

adequate calories and protein are being supplied by the breast milk. After this, when prolonged breast-feeding and small supplementary feeds of carbohydrate are continued with, it is usual for the growth curves to become definitely retarded as compared with Caucasian standards (Meyers, 1951). This is partly the result of the child's struggle for malarial immunity, which occurs at this time, but is probably mainly due to the fact that even normal breast milk, with occasional feeds of carbohydrate, is not sufficient to supply the calorific and, particularly, the protein demands of the growing infant. While the present investigation has suggested that the breast milk of poorly nourished African mothers contains a comparatively normal content of protein, it is of course possible that some other factor may become deficient, or more likely that the actual yield diminishes when lactation is prolonged. Albanese (1951) has analysed the same problem in Chinese infants, and believes that the retardation of the curve is probably due to a quantitative rather than a qualitative milk deficiency, while recent work in Ibadan, when breast milk has been manually expressed from lactating African women, has suggested that a poor yield occurs (Jelliffe, 1952b).

At the Inter-African Conference on Nutrition (1949) it was estimated by the Belgian delegation that the *per capita* supply of animal protein for the Congo as a whole was less than 5 g. a day. It is certain that similar figures apply in most tropical African countries, and recent food analyses in Ibadan by Woodruff (1951) have shown that it is unusual for pregnant women to have more than 1 oz. (28 g.) of animal protein every three or four days, while many only have about 1 oz. each week. In addition to this, their diet was also shown to be very deficient in non-animal protein. It has been found (National Research Council of the United States, 1945) that during normal lactation 8–12 g. of protein will be secreted daily, which represents 8–12% of the protein intake usually recommended for the average pregnant woman —namely, 100 g. (Clements, 1949). At the present state of knowledge it is difficult to understand how the malnourished African nursing mother is capable of producing milk of such high protein content for so long under such adverse dietary conditions. It is, however, of interest to note that experimental work with goats and cows has suggested that it is the globulin of the serum that provides most, if not all, of the nitrogen for the synthesis of milk protein (Petersen, 1944). As Clements (1949) observes, if the same mechanism holds for human milk, the supply of serum globulin must be maintained at a satisfactory level if the demands of the mammary tissue are to be met. It has been emphasized by numerous observers (Mohun, 1946; Stephen, 1948; etc.) that, for reasons largely unknown, the plasma proteins of Africans, as of Fijians (Wills and Bell, 1951) and other tropical peoples, tend to be particularly high in globulin, despite the poor intake of amino-acids.

The relatively normal protein found in the present survey re-emphasizes the fact that under present conditions in tropical Africa the custom of prolonged breast-feeding should be continued with, as the alternative is an early weaning on to a diet of carbohydrate pastes and almost no protein. Prolonged breast-feeding should, however, be combined with early and adequate supplementary feeds of the most easily digestible carbohydrate foods, and, in addition, such locally produced protein foods as are available (eggs, beans, goat's milk, etc.).

Summary

Seventy-six specimens of breast milk from Nigerian nursing mothers were analysed to determine the protein content. The average was found to be 1.04% (range 0.59% to 1.76%). The length of lactation varied from 1 to 36 months. No evidence was found of a decrease of the protein content with prolonged lactation. The results are believed to compare favourably with those from other parts of the world.

My thanks are due to Mr. LaMar N. BeMiller and Mrs. Theodora Bonham, of the Mead Johnson Research Laboratories, Evansville, U.S.A., for undertaking the actual analyses, to Miss Mary Devereaux for library assistance, and to Miss Morell, of Tulane Medical School, New Orleans, for drawing the "scatter-diagram."

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FAILURE OF MASSIVE DOSES OF VITAMIN B_{12} IN ACUTE LEUKAEMIA

BY

IAN WELSH, M.B., B.Ch., B.Sc.
University of Witwatersrand; Nuffield Dominion Travelling Fellow, Nuffield Department of Medicine, Oxford

This trial of vitamin B_{12} in acute leukaemia was carried out at the suggestion of the Medical Research Council. Clinical workers had reported the apparent occurrence of remissions in patients with malignant disease who had been treated empirically with vitamin B_{12}. It was conceivable that vitamin B_{12} might promote the differentiation of leukaemic cells into normal leucocytes, on the analogy of the restoration of normal blood formation in pernicious anaemia. Messrs. Glaxo Laboratories made available a supply of vitamin B_{12} in ampoules containing 1 mg., which is approximately 1,000 times the maintenance dose in pernicious anaemia. The dosage decided on was 1 mg. intramuscularly a day, regardless of the type of the acute leukaemia or the age of the patient.

The co-operation of physicians and clinical pathologists in the Oxford region enabled us to treat and follow up 25 unselected cases of acute leukaemia in less than a year. Diagnosis was made on clinical and blood findings and confirmed by marrow aspiration. Marrow puncture was repeated in the few cases in which the peripheral blood showed much change. The cases were not divided into treated patients and untreated controls, because the usual course of acute leukaemia, including the frequency of partial and complete remissions, is now well known (Bierman *et al.*, 1950; Southam *et al.*, 1951), and any important modification as a result of treatment should soon become apparent. The prescription of blood transfusions and antibiotics was left to the discretion of the physician in charge of the patient, but other remedies such as *x* rays, radiomimetic drugs, A.C.T.H., and cortisone were not used.

The results are shown in the Table. The patients treated consisted of 11 females and 14 males, their ages varying between 3 and 69 years; 10 were 14 years of age or less, and the average age was 25 years. The cell types were as follows: 10 acute myeloblastic or myeloid, six undifferentiated cell type, five lymphoblastic, and four monocytic. The average time from onset of symptoms to diagnosis was approximately seven weeks. The survival after diagnosis ranged from 156 days to 2 days, with an average of 52 days. The total duration of the disease thus averaged about 14½ weeks, and there were no instances of noticeably long survival.

Results of Treatment

No.	Sex	Age in Years	Diagnosis	Duration of Symptoms Before Diagnosis	Survival After Diagnosis in Days	Total B_{12} in mg.	Partial Remission
1	F	4	Acute undifferentiated	8 weeks	156	68	+
2	M	40	Acute myeloblastic	2 ,,	130	130	+
3	F	4	,, undifferentiated	10 ,,	120	48	+
4	F	17	Acute monocytic	12 ,,	103	103	0
5	M	69	,, ,,	8 ,,	96	96	0
6	M	63	,, myeloblastic	14 ,,	90	16	0
7	F	29	,, monocytic	3 ,,	90	65	+
8	M	4½	,, lymphoblastic	2 ,,	70	70	+
9	M	3	,, ,,	8 ,,	65	60	+
10	F	3	,, stem cell	12 ,,	62	56	0
11	M	30	,, monocytic	12 ,,	58	48	0
12	M	14	,, myeloblastic	4 ,,	45	45	0
13	M	22	,, undifferentiated	2 ,,	44	44	0
14	M	3½	Acute lymphoblastic	4 ,,	40	40	0
15	M	56	,, ,,	3 ,,	35	35	0
16	M	23	,, myeloid	? mths	21	21	0
17	F	19	,, ,,	? ,,	18	18	0
18	M	4	,, ,,	3 weeks	11	11	0
19	F	43	,, myeloblastic	9 ,,	8	8	0
20	F	54	,, myeloid	5 ,,	8	8	0
21	F	47	,, lymphoblastic	16 ,,	6	6	0
22	M	30	,, myeloblastic	8 ,,	6	6	0
23	F	41	,, erythraemic myelosis	3 ,,	5	5	0
24	M	14	Undifferentiated	4 ,,	5	5	0
25	F	3½	,,	12 ,,	2	2	0

All the patients are now dead. None showed a complete remission; the nearest was Case 2, who had a good clinical remission lasting three months, during which time his blast cells dropped from 20% to 5%, but the haemoglobin did not rise above 60% and the platelet count remained at 50,000 per c.mm.

No patient became apyrexial on treatment, nor was there any substantial retrogression in the size of the spleen or glands. Only objective signs of clinical improvement, such as gain in weight or rise in haemoglobin, have been recorded. Six cases (Nos. 1, 2, 3, 7, 8, and 9) had a partial remission, and an additional 10 felt better but did not show any objective change in their condition. No toxic effect attributable to the B_{12} was observed.

Summary

Twenty-five patients with acute leukaemia have been treated with massive doses of vitamin B_{12}. None lived for more than five months after beginning treatment. No complete remissions occurred, but six patients had partial remissions and a further 10 reported feeling better.

There is no evidence from this series to suggest that the prognosis or clinical course of acute leukaemia is altered by adding vitamin B_{12} to other treatment.

Thanks are due to Professor L. J. Witts, in whose department much of the work was performed and whose help is gratefully acknowledged; to Messrs. Glaxo Laboratories for a generous supply of vitamin B_{12}; and to the physicians and clinical pathologists of the Oxford region for their co-operation.

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USE OF A.C.T.H. IN AGRANULOCYTOSIS

BY

H. FULD, M.D., M.R.C.P.Ed.
Physician, Sefton General Hospital, Liverpool

The papers by Discombe (1952) and by Dudley Hart *et al.* (1952) prompt me to publish the following notes. In the former article the relatively frequent occurrence of agranulocytosis on the Continent is compared with the rarity of the condition in this country, and is explained by the popularity which amidopyrine has gained and still maintains outside Great Britain. My own experience (Fuld, 1931) of having observed three fatal cases of agranulocytosis within six months in 1930 in a medium-sized German hospital where "pyramidon" (amidopyrine) was the standard drug, only second to aspirin in its frequency of administration, supports Dr. Discombe's conclusions. This is, however, only in retrospect, as I was quite unaware of the relationship of amidopyrine to agranulocytosis at that time.

In the past 19 years I have, of course, come across a number of patients with more or less severe leucopenic reactions following sulphonamides and thiouracil preparations, but no true case of agranulocytosis was met with until May, 1952.

Case Report

A woman aged 65 was referred by her doctor on May 30, 1952. She had had remarkably good health until a year previously, when she compained of lack of energy and

general weakness which had persisted ever since. Her appetite had deteriorated during the last three months. In March she had a short course of sulphonamides for a septic finger, and again ten days later for a boil on her back which never healed properly. She did not notice any change in her general condition before and after this treatment. During the last few weeks she rested a good deal, but was not entirely confined to bed.

On examination she appeared a rather pale thin woman with evidence of recent loss of weight. Apart from a radiologically confirmed slight enlargement of her heart and a systolic apical murmur there were no significant changes in her cardiovascular system. Her palate was granular. There were no ulcers in her mouth or pharynx. Her spleen reached 1 in. (2.5 cm.) below the costal margin, and was hard. Her blood count on May 30 was: red cells, 2,550,000; haemoglobin, 48%; colour index, 0.94; white cells, 600 (polymorphs 3%, lymphocytes 78%, monocytes 19%). *X*-ray films of the skeletal system showed Paget's disease of the right femur.

A diagnosis of agranulocytosis was made, and she was put on treatment which included "cytamen," iron, folic acid, ascorbic acid, the vitamin-B complex reinforced by pyridoxine, as well as blood transfusions (2 pints (1.1 litres) on June 4 and on June 24). She also received large doses of penicillin, and, in the later course of her illness, streptomycin. On June 3 her peripheral count had not materially altered: red cells, 2,580,000; haemoglobin, 49%; colour index, 0.96; white cells, 650 (all lymphocytes). Her bone-marrow count consisted of: blast cells, 0.5%; premyelocytes, 1%; myelocytes, 29%; metamyelocytes, 4%; neutrophil polymorphs, 0.5%; eosinophils, 0.5%; normoblasts, early 3.5%, intermediate 11.5%, late 4.5%; monocytes, 2%; lymphocytes, 43%. The myeloid/erythroid ratio was 1.8:1.

On June 11 her white cells numbered 950 without any lymphocytes being seen. On June 19 her red-cell count was 3,220,000; haemoglobin, 59%; colour index, 0.9. There were 800 white cells, all lymphocytes. On June 23 her temperature rose rather high and remained so for three days in spite of antibiotics. An irritating laryngitis and tracheitis had developed and there was a small clean ulcer on her hard palate. On June 24 her white cells numbered 600. No granulocytes were seen.

A.C.T.H. was started on June 25, and for six days she received 20 mg. six-hourly. On July 1 the dose was cut to 20 mg. twice daily, and the treatment was stopped after a total of 600 mg. had been given in nine days. After 140 mg. of A.C.T.H. had been injected the bone-marrow content was: myelocytes, 16%; metamyelocytes, 13%; neutrophils, 2%; lymphoblasts, 2%; lymphocytes (large and small), 60%; normoblasts, early 1%, intermediate 4%, late 2%. At that time she had 500 white cells per c.mm., with 6% neutrophils and 94% lymphocytes in her peripheral blood. On the sixth day of treatment with A.C.T.H. her temperature again rose and she developed laryngitis and diarrhoea, which did not respond to antibiotics. On the eighth day her peripheral blood count was: red cells, 2,600,000; haemoglobin, 54%; colour index, 0.9; white cells, 450. No granulocytes were seen.

A.C.T.H. was stopped on July 3, as neither the patient's general condition nor her bone-marrow function or peripheral blood showed evidence of recovery. She was again put on the remedies which were given before the trial with A.C.T.H., but her condition steadily deteriorated and the last blood count taken on July 11 (20 hours before her death) revealed only 200 white cells with complete absence of granulocytes. She still maintained her red-cell and haemoglobin level. Her temperature reached 104° F. (40° C.), and the diarrhoea persisted. Pericardial friction rubs were heard and she developed oedema of the legs. On the evening of that day she sank into coma and died in the early morning hours of July 12.

Conclusions

This patient had been ill for many months before she came under observation, and I believe that her blood disorder existed before sulphonamides were prescribed. Neither antibiotics nor A.C.T.H. had any appreciable effect on the outcome.

I believe that this case belongs to the group of idiopathic agranulocytosis cases which appear to remain unaffected by A.C.T.H. Caldwell (1950) and McMillin (1951) both deal with drug-induced cases of agranulocytosis successfully treated by A.C.T.H. and cortisone respectively. Dudley Hart *et al.* wrote with reference to A.C.T.H. or cortisone that "they may act only in some cases of acute drug-induced agranulocytosis." My own experience entirely supports their opinion.

Idiopathic agranulocytosis, first described 50 years ago, still remains a problem so far as aetiology is concerned and a challenge in respect to treatment.

Summary

A case of agranulocytosis of unknown origin is described. The patient failed to respond to treatment, which included A.C.T.H. over a period of nine days.

The prognosis for agranulocytosis of unknown aetiology remains grave in spite of the introduction of cortisone and A.C.T.H.

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Medical Memoranda

Fractured Shaft of Femur Complicated by Multiple Systemic Emboli

CASE REPORT

A policeman aged 41 was admitted to hospital on March 4, 1951, having fallen sideways off his bicycle on to his left hip, and sustaining a comminuted fracture of the upper third of the left femur. At the time there was no evidence of a nerve or vascular lesion. *X*-ray films showed a comminuted pertrochanteric fracture of the femur, with a long posterior fragment. A Steinmann pin was inserted into his tibial tubercle and a balanced skeletal traction set up. It was thought, because of the comminution, that closer apposition of the fragment could be obtained by applying a clamp to the Thomas splint. This did, in fact, improve the alignment.

At 7.40 a.m. on April 4, exactly a month after admission, he had a sudden right hemiplegia. This cleared up rapidly, and when seen again at 11 a.m. he had only a residual right facial weakness. His blood pressure was 100/80. Dr. Kemball Price thought the condition was due to an embolism. At 5 p.m. the patient complained that his right leg was cold and painful for an hour. On examination the right leg felt cold and there was complete paralysis of all his muscles below the knee. His right popliteal fossa and calf were extremely tender. The posterior tibial and dorsalis pedis arteris could not be felt. A diagnosis of popliteal embolus was made.

Operation.—At 8 p.m. skeletal traction was converted into fixed traction and a spinal anaesthetic was given. Exploration of the popliteal vessels was carried out through a long midline incision. It was noted that after the induction of anaesthesia vasodilatation did not occur in the right leg, although it did in the left. The popliteal vessels were exposed. The popliteal artery felt hard and was white. It was opened and a 3-in. (7.6-cm.) clot removed. This, however, was not followed by a sudden spurt of blood from the proximal end, and it was not until the last piece of the clot was removed from the portion of the artery which lay in Hunter's canal that the artery was found to be clear. The

incision in the vessel was sutured with arterial-silk atraumatic needles. All the instruments and the wound were washed with sodium citrate.

Post-operatively he was given 15,000 units of heparin through a polythene tube six-hourly. At 2 a.m., five hours after the operation, I was called to see him because of persistent oozing. This was not severe, and not unexpected in view of the spinal anaesthetic. It was noted at this time, however, that he had made a complete recovery from the paralysis and could actively dorsiflex and plantar-flex his foot. Both his lower-limb pulses had returned. Transfusion was considered because of loss of blood during and after operation and because of the necessity for an adequate blood pressure to maintain a good popliteal circulation, but in view of the recent hemiplegia it was thought inadvisable at that stage.

On April 9 much oedema was present from the popliteal fossa downwards, but there was no evidence of aneurysm. Next day an electrocardiogram showed atrial infarction. This no doubt accounted for the source of his emboli. On the 11th his leg suddenly went blue about half an hour after an injection of heparin. As this was thought to be due to haemorrhage with compression of the vessel, 15 ml. of protamine sulphate was given intravenously. It was decided that in order to try to save his limb a blood drip should be set up.

On April 24 the swelling had gone down, but he had complete sensory-nerve loss from the knee downward. His red cells numbered 3,750,000 and the haemoglobin was 68%. The condition of his leg gradually improved. First protopathic sensation and then epicritic sensation returned.

A final examination on July 4 showed some wasting of the calf muscles and a slight equinus deformity due to fibrosis. He was able to walk fairly well with a raised heel and a toe spring.

I am greatly indebted to Mr. J. M. Turner and Mr. H. J. McCurrich for their permission to publish this case.

W. LAURENCE, F.R.C.S., F.R.C.S.Ed.,
Senior Orthopaedic Registrar,
Brighton and Lewes Hospital Group.

Acute Pethidine Poisoning

In a search of the literature only one case has been found where pethidine has been taken with suicidal intent. The satisfactory response to treatment also makes the following case interesting.

CASE REPORT

A married woman aged 43 had suffered from tuberculosis of the bladder for 20 years. She had had a left nephrectomy 20 years ago. Because of the pain and frequency, admission to hospital was arranged for July 22, 1950. She had previously refused to come into hospital, but eventually agreed, stipulating a Saturday. Owing to the shortage of beds it was necessary to cancel this carefully arranged admission at the last minute. The same day she was found unconscious at home. She was brought to hospital accompanied by her mother. The mother's account and the patient's appearance indicated that she was suffering from a narcotic poison. The mother had not brought the remaining tablets, so was sent to fetch them, having identified a tablet of phenobarbitone, 1 gr. (65 mg.), as being similar to those in the box.

The patient was found to be deeply comatose, and there was no response to pressure on the supra-orbital nerves nor to any other stimuli. There was extreme respiratory depression, the rate being 16 per minute and very shallow; pulse rate 90 per minute; temperature 97° F. (36.1° C.); blood pressure 100/65; no sweating. The pupils were equal and contracted, with no response to light, and no tendon jerks were present. There were no plantar reflexes, and no other relevant findings.

TREATMENT

It was clear that whatever tablets had been taken they were not aspirin. Phenobarbitone is the commonest agent in attempted suicide by drugs, and the pupils were contracted. (Opinions vary on the state of the pupils in barbitone poisoning, but from personal observation the pupils are more often contracted than dilated.) The patient's condition called for immediate treatment, and, as her mother had not returned with the tablets for identification, treatment had to be empirical. She was given picrotoxin, 6 mg. intravenously, with no effect. This was followed two minutes later by amphetamine sulphate, 60 mg. intravenously, with no effect. Three minutes later nikethamide, 6 ml., was given intravenously. In *thirty seconds* the patient became conscious. Although a little confused she recognized her surroundings, and when questioned immediately replied that she had taken 30 tablets of pethidine (1,500 mg.), as she was "fed up." Her mother then arrived with the box of tablets, which were confirmed as pethidine; 20 of the original 50 remained. The patient was now very emotional and would not co-operate in having her stomach washed out. No further treatment was given, but there was no sign of her relapsing back into coma. At 8.30 p.m. she was sweating and shocked. She had a disturbed night (doubtless due to the amphetamine sulphate), but the next morning she was normal again.

Pethidine is rapidly absorbed, quickly metabolized, and partially excreted unchanged in the urine. Elimination of the ingested pethidine was studied by analyses of urine collections, using the method of Lehman and Aitken (1943), with the following results: 6.7 mg. (49th to 73rd hour after ingestion), 2.8 mg. (81st to 105th hour), 0.6 mg. (105th to 129th hour).

DISCUSSION

The absence of vomiting and sweating in the case reported here is noteworthy. The pupils were small, which is unexpected, as in therapeutic doses pethidine causes mydriasis. Recovery was complete within 24 hours. Way (1946) has pointed out that pethidine may stimulate or depress the central nervous system. With overdoses it is the stimulatory action that is usually seen (for example, tremors, uncoordinated muscular movements, and, experimentally, epileptiform seizures), but in certain individuals (as in this case) the depressant action may predominate.

Cases of acute poisoning by pethidine are few. Experimentally, death results from respiratory failure (Gruber *et al.*, 1941). Polonio (1947) mentions two patients with pethidine addiction who had several crises of respiratory failure which responded well to nikethamide. In two deaths which he observed, necropsies could not be made but "the history and post-mortem appearance of cyanosis and engorged veins alike indicated respiratory failure." The only case found of pethidine being taken with suicidal intent is reported by Cohen (1950).

Nikethamide counteracts the effect of depressants of the central nervous system, but how it does so is obscure. From personal experience it is useful in interrupting pentothal narcosis, the treatment of phenobarbitone poisoning, and acute alcoholism. In this case it was dramatically effective in terminating the coma and respiratory depression, and, although one might have expected a relapse into coma, no further injection was necessary. Perhaps the amphetamine sulphate contributed to the sustained recovery of consciousness. As nikethamide is effective in correcting depression of the central nervous system from such different causes, this suggests that, when confronted with a coma from suspected but unknown poisoning, an empirical trial, as in this case, is well worth while.

I am grateful to Dr. H. L. Milles, under whose care the patient was, and to Mr. H. B. Salt, biochemist, for his help with the urinary estimations.

C. ROMER, M.B., B.S.

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Reviews

UROLOGICAL PATHOLOGY

Urological Pathology. Volumes 1 and 2. By Peter A. Herbut, M.D. (Pp. 1,222; 527 illustrations, including 2 in colour. £8 10s.) London: Henry Kimpton. 1952.

The appearance of a two-volume work of more than 1,200 pages which deals mainly with the pathology of diseases of the urinary tract is an indication of the rapid growth of the specialty of urology. The authors of previous large volumes have considered the subject more from the clinical and therapeutic standpoint; in this work the pathological aspect is used as a basis for description, although the clinico-pathological correlation is also detailed, and brief indications of the methods of treatment and the prognosis are included. They serve, as the author wishes, to broaden the usefulness of the book.

The author has adopted a regional basis in setting out the pathological conditions encountered. This leads to some repetition, but it makes the work of more value for reference. The same systematic subheadings are used throughout, and it is quickly evident that a vast amount of methodical work has been put into its preparation. The sections on embryology call for special mention, and as a natural sequence of their excellence the congenital deformities of the urinary and genital tract are well described; there is not, however, as yet a satisfactory explanation of the genesis of epispadias. Another chapter worthy of praise is that on the adrenal glands; the author defines clearly the different varieties of tumour and their hormonal effects. There is no mention of the finding of an excessive amount of *nor*adrenaline in the urine as a diagnostic test in phaeochromocytoma; possibly it is too recent for inclusion. There are few other omissions, but an important one is on the occurrence of hyperchloraemic acidosis in some cases of uretero-colostomy. The illustrations are good and plentiful; those taken from *Gray's Anatomy* give the pages a familiar aspect. There is a very full bibliography at the end of each section, and it is pleasing that this does not neglect British references.

This is one of the most important works on the special pathology of the urinary tract ever published. While it is probably too full for the student or general practitioner, its possession as a volume of reference is essential to every urologist.

E. W. RICHES.

PROSTATECTOMY

Prostatectomy: A Method and its Management. By Professor Charles Wells. (Pp. 103; 73 illustrations. £1 4s.) Edinburgh and London: E. and S. Livingstone. 1952.

The progress made in surgery in recent years is attributed mainly to advances in anaesthesia, control of sepsis, and a better understanding of the body's needs of fluid, proteins, and electrolytes: it is upon these principles that the technique described in this book has been developed. The type of prostatectomy which best fulfilled the author's requirements was that devised by Wilson Hey, and it is this operation which he has adopted with slight modifications.

An interesting review of the historical background of operations on the prostate gland is followed by a short description of the pathology of the gland and of the organs of the upper urinary tract as they are affected by bladder-neck obstruction. The investigation of such cases is restricted by the rigid prohibition of instrumentation, so that their assessment depends on palpation, urine and blood examination, and intravenous pyelography. It is upon these findings that the indications for treatment are based. The author groups the cases in three classes; for the first two—acute retention of sudden origin and acute retention superimposed on chronic retention—he makes strong claims for immediate operation, while for the third—chronic retention—he considers enucleation of the prostate to be the only method of obtaining adequate drainage of the kidneys. The method of anaesthesia is especially designed to maintain the blood pressure without increasing the loss of blood at the site of operation. The author describes the operation in detail, and each step is admirably illustrated by photographs and drawings. The after-treatment is mainly concerned with maintaining renal secretion and control of sepsis.

But it is the two final chapters which make this book outstanding. The one on high degrees of chronic retention clearly indicates the causative factors and how they should be treated, while the other, on fluid, electrolytes, and proteins, describes very clearly the effects of renal impairment, and how abnormalities may be recognized and adjusted.

J. E. SEMPLE.

REVIEW OF CYTOLOGY

International Review of Cytology. Volume 1. Edited by G. H. Bourne and J. F. Danielli. Prepared under the auspices of the International Society for Cell Biology. (Pp. 368; illustrated. $7.80.) New York: Academic Press, Inc. 1952.

In a foreword, the editors of this book remark that the volume of published research on cell biology has now become so great that it cannot be covered by any individual without the help of a regular review service. The *International Review of Cytology*, published under the auspices of the International Society for Cell Biology, is designed to provide the needed help. The editors intend by annual publication to cover the whole field of cytology and cell biology, over a period of years, in papers contributed, by invitation, by experts in all parts of the world. They propose to seek critical discussions of published work and to welcome articles presenting new theories of general interest. For the first volume they have collected 16 articles greatly varied in subject and in treatment. They range from highly individual theoretical discussions to detailed, well-documented reviews of technical procedures such as the applications of freeze-drying, staining, and electron microscopy to cytological research. Several articles are purely biochemical. Others are on a diversity of subjects, including bacterial cytology, nucleo-cytoplasmic relations in amphibian development, the cytology of mammalian epidermis and sebaceous glands, and the behaviour of spermatozoa in the neighbourhood of eggs.

The demand for annual reviews is outstripping the supply of expert reviewers. The writing of a comprehensive and critical review is an exacting and laborious task. Some contributors to the present volume grapple with the task conscientiously and effectively; others scarcely attempt it. Stricter editorial control seems needed if the new *Review* is to acquire a distinctive character. The theoretical discussions by eminent writers are of great interest, but more of the detailed factual reviews would probably be of greater service to the general reader. In future years, no doubt, the *Review* will settle down to a more circumscribed field and, avoiding uniformity, achieve a unity which the first volume lacks. Meanwhile it is welcome for factual information and stimulating ideas, and goes far to supply an evident need.

L. FOULDS.

OSTEOARTHRITIS OF THE HIP

Osteo-arthritis of the Hip: with special reference to Treatment by Vitallium Mould Arthroplasty. By W. Alexander Law, O.B.E., M.D., F.R.C.S. (Pp. 87; 31 figures. £1 5s.) London: Butterworth and Co. 1952.

The essay which won the coveted Robert Jones Prize of the British Orthopaedic Association for 1950 has now appeared in book form. It makes a slim volume with only 44 pages of actual text, but not a word wasted; most of the 31 pages of illustrations consist of single large radiographs. In the first half the author gives a useful general review of osteoarthritis of the hip-joint and various methods of treatment. Vaccines, deep *x* rays, injections of acid, and

sensory denervation of the joint are all damned with faint praise. The second half contains a careful record of the author's experience of cup arthroplasty in a personal series of 160 patients, of whom 44 required operation on both sides. It is written with a measure of enthusiasm which is fully justified by the regular alleviation of pain and truly impressive figures for the average final range of movement. By 1950, however, the subject of reconstruction of the hip-joint had already been covered in great detail by Smith-Petersen and his pupils, including Mr. Law, and with reports of similar results. For this reason those who have kept up with orthopaedic literature will find in this essay little that is quite new; those who have not will find much.

In a way the book marks the end of a decade during which the revolutionary technique of Smith-Petersen was hardly challenged, at any rate in the English-speaking world. But Continental surgeons would be surprised to hear that an essay on this subject could have gained such a high award without some tentative appraisal of the merits and the demerits of the acrylic prosthesis designed by the Judet brothers. They might indeed refer to Postel's monograph which appeared in 1951 from the service of Professor Merle d'Aubigné at the Hôpital Cochin, and which compares the early results of both methods in a total number of 135 cases. (Postel finds little between them, but, like the general run of orthopaedic surgeons, he complains that 20% of patients are not relieved to a worthwhile extent by either procedure.)

For the last few years the treatment of osteoarthritis of the hip-joint has been in a state of turmoil: there have been so many new techniques, both conservative and operative. How many of them will survive the next 10 or 20 years—that is the question. Truly there is some point to the quotation from St. Chrysostom with which Mr. Law introduces his essay: "It is not names which give confidence in things, but things which give confidence in names."

K. I. NISSEN.

JOINT MANIPULATION

The Science and Art of Joint Manipulation. By James Mennell, M.A., M.D., B.C.(Cantab.). Volume 2: *The Spinal Column.* (Pp. 264; 148 illustrations, many in colour. £2 2s.) London: J. and A. Churchill. 1952.

This is the second volume of Dr. Mennell's work on the manipulative treatment of certain joint affections, the first volume of which (*The Extremities*) has already reached its second edition. The author's aim has been to put joint manipulation on a sound scientific basis and to assess its true value. He has hoped thereby to remove the prejudice that has grown up in the minds of many medical men against manipulative treatment—a prejudice that exists largely because no satisfactory explanation has been offered of why manipulation succeeds.

Dr. Mennell himself rejects the theories of the unqualified practitioners which are so often at variance with pathological observation. He believes that many joint pains—and many pains arising from joints but referred to other parts—are caused by "binding" of the opposing joint surfaces, and that when this is so the pain can be abolished or relieved by freeing the joint by manipulation. He appreciates fully the importance of careful diagnosis, demanding an exhaustive discovery of the history and painstaking clinical examination. He accepts also the need for radiographic examination before treatment by manipulation is considered.

These aspects of the problem occupy a large section of this new volume, which incorporates an earlier book entitled *Backache.* All will commend the author's clear description of his methods of clinical examination of the spine, from which there is much to be learnt. But many of his deductions will be unacceptable to orthopaedic surgeons—especially his scepticism of the significance of disk extrusion as a cause of sciatic pain, his claim that "binding" of a sacro-iliac joint is often responsible for sudden agonizing sciatica and "sciatic" scoliosis, and his belief in "tight fascial bands" in the thigh or calf as sources of limb pain. He is, of course, fully entitled to his views, but they are clearly based on hypothesis and not on pathological study. The same criticism can be directed against his basic assumption that joint surfaces "bind" together and thus cause symptoms correctable by manipulation. On the other hand the section of the book devoted to the technique of joint manipulation deserves nothing but praise. The descriptions are clear, well written, and well illustrated by numerous simple line drawings and photographs.

The book is strongly recommended to those who wish to learn how to manipulate the joints of the spine. Those who would learn when to manipulate, or why manipulation sometimes succeeds, must approach it with an open mind and judge for themselves whether or not the author's arguments are convincing.

J. C. ADAMS.

LIFE OF FLEMING

Fleming: Discoverer of Penicillin. By L. J. Ludovici. (Pp. 223. 15s.) London: Andrew Dakers. 1952.

On August 6, 1881, in a moorland farmhouse set in the hills of Ayrshire, was born a babe who was destined to have a remarkable effect on the future physical well-being of mankind. Alexander Fleming, the youngest of eight children, was educated first at a tiny moorland school near his home, then at Darvel school, which meant a long tramp of four miles each way daily, and finally at Kilmarnock Academy, where he made rapid progress. At the age of 14 he came to London to stay with his doctor-brother, and two years later he entered a shipping office with a view to a commercial career. Four years later, however, he was left a legacy, and his brother advised him to study medicine. He was a strong swimmer and a fine water-polo player and had played against St. Mary's team, and this fact decided him to study at St. Mary's Hospital Medical School.

It was a fateful decision, for at that time Almroth Wright had just been appointed bacteriologist to the hospital and lecturer in the medical school. Wright had a breadth of knowledge, a depth of culture, an ingenuity of experimental resource, a powerful imagination, and a wonderfully persuasive gift of tongues, and this rare combination enabled him to found a school of research which soon influenced, as it is still influencing, the medical world. Fleming had a distinguished academic career, and as soon as he qualified he went to work with Wright. Inspired and guided by his master, he soon showed wonderful experimental dexterity and acute power of observation, which he demonstrated in his work on antiseptics and the various protective powers of the blood. His discovery of lysozyme and later of penicillin were both the results of his genius for accurate observation. The delay in the development of the latter substance was not due to any failure on his part to point out all its remarkable qualities. Fleming himself has said that "the resuscitation of penicillin as a chemotherapeutic remedy is due to the brilliant work of Florey and his colleagues at Oxford." Nevertheless the name of Fleming will rightly always be associated with the discovery of penicillin, which has not only transformed the scope and safety of surgery but has opened a new field of therapeutic resource.

Fleming has always been a modest man of quiet demeanour, and, though it is natural that the public should want to know as much as possible of such a famous man, it is also true that the quietude of a laboratory does not lend itself well to popular description. Nevertheless, Mr. Ludovici has done his best to make bacteriological experiments interesting to the public and has given many interesting details of the career of his famous subject. But there is much repetition and too much straining after effect, and the proofs were not read carefully. The fame of Alexander Fleming is secure, but this book is unlikely to be the definitive biography.

V. ZACHARY COPE.

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY NOVEMBER 22 1952

SKIN DISINFECTION

Antiseptics are probably more commonly applied to the skin before puncture or incision than for any other purpose. In view of the immense scale of this form of use and of its importance in preventing sepsis it is surprising that such a variety of substances are still used for this purpose. They belong to at least five main classes—alcohols, halogens, mercury compounds, dyes, and quaternary ammonium compounds. Presumably some of these are more effective than others, but the surgeon may be forgiven for making his own choice, since vigorous advocates of each method are to be found in the medical literature, and without an extensive knowledge of bacteriology it is impossible to see the flaw in the test method used which so often vitiates the results. The testing of disinfectants generally abounds in pitfalls, and skin disinfection is one of its most difficult branches. A great variety of methods has been used, none of which has gained general acceptance, and the apparent facility of such tests and their direct interest to the surgeon have led many amateurs to explore this field with the contradictory results which we see.

It is generally agreed that the entire removal of the resident skin flora is neither possible nor necessary: the aim of disinfection is to destroy transient surface flora which may include pathogens. An appropriate method of test is therefore one in which a specific pathogenic organism is applied to the skin and efforts are made to eliminate it. Dr. P. Story, whose paper on this subject appears on page 1128, has introduced an ingenious method for confining observations to the organism deliberately applied. Most of his tests were made with a highly penicillin-resistant strain of *Staph. pyogenes*, and the medium used for cultivation contained penicillin in a concentration to which this staphylococcus was indifferent, although it served to suppress the growth of all the normal skin flora. It was thus possible to enumerate survivors from among the staphylococci applied to a measured area of skin at intervals after treatment, without interference by the resident bacteria.

The results confirm in the first place an observation on which almost all reliable workers are unanimous—namely, that tincture of iodine is highly and rapidly effective. But there are several objections to the use of iodine, and it is important to know whether anything else will serve as well. Of the other disinfectants tested, only 70% spirit, used either alone or as a solvent, consistently achieved "virtual disinfection" in 30 seconds, not only when the test organism was *Staph. pyogenes* but in tests with three species of Gram-negative bacilli. The virtues of alcohol as a skin disinfectant have not been disregarded in the past; among authors reporting various tests showing its superiority have been Archer[1] in this *Journal*, Hatfield and Lockwood[2] in the United States, Neufeld[3] in Germany, and Hirsch[4] and Sobernheim[5] in Switzerland. Several of these authors have compared the action of alcohol with that of quaternary ammonium compounds with results unfavourable to the latter; the writings of Neufeld in particular form part of a polemic in which the utility of these substances has been hotly disputed. They are said to form a film over the skin beneath which bacteria survive. They certainly, like mercury compounds, inhibit the growth of surviving bacteria which have been exposed to them in extreme dilution, so that any ordinary test will credit them with bactericidal power which they do not possess. It is for this reason that so much published information about these two classes of disinfectant is spurious.

In order to enable exposed but surviving bacteria to multiply as they undoubtedly can in the body it is necessary to neutralize the disinfectant inevitably carried over in the culture which determines the result. Of many substances which have been recommended for this purpose, that used by Story was a suspension of milk powder, and this enabled survivors to grow, except when the disinfectant was used in a concentration as high as 10%. Cetrimide, perhaps the best known "quaternary" in use in this country, did not achieve virtual disinfection regularly when used in aqueous solution in concentrations of 1% and 2%, even in experiments with staphylococci, which are much more susceptible to it than other bacteria. Two other well-known substances of this class, "zephiran" (the prototype of the quaternaries, originally described by Domagk) and "bradosol," gave similar results in a smaller number of tests. It could not be claimed that these few unpromising findings do more than indicate a need for further inquiry. There are many of these compounds on the market, and there is singularly little information about their relative merits. If, as was recently stated in this *Journal*,[6]

1 *British Medical Journal*, 1945, **2**, 148.
2 *Surgery*, 1943, **13**, 9310.
3 *Z. Hyg. InfektKr.* 1943, **123**, 396; **124**, 751; **125**, 287.
4 *Schweiz. med. Wschr.*, 1950, **80**, 1285.
5 Ibid. 1943, **73**, 1280, 1304, 1333.
6 *British Medical Journal*, 1952, **1**, 1260.

some of them are much more active than others, even against so resistant an organism as *Ps. pyocyanea*, a full account of comparative tests in which these differences are established would be of great interest and value. It should help to define the true utility of these disinfectants for various clinical purposes, which at present, despite the great volume of already published information, must be regarded as not altogether settled.

CARCINOMA OF THE THYROID

Radioactive iodine has now become an essential adjunct in the treatment of thyroid carcinoma whenever surgical excision of the tumour cannot be complete and when metastases are present. This is especially so when the tumour is a well-differentiated one, for the probability of successful isotope treatment is then much greater. There have been a number of reviews on this subject in recent years, and, although the statistics in England and Wales show that death from thyroid cancer is not very common,[1] yet many patients have now been given successful palliative treatment with radioactive iodine,[2 3] sometimes with remarkable improvement.[4 5] The thyroid gland appears unique in its capacity to produce metastases, histologically resembling normal thyroid tissue, and this new therapeutic measure can thus be used to treat them.

In the opening pages of this issue Dr. E. E. Pochin and his associates at University College Hospital describe the indications for radio-iodine treatment in thyroid cancer. They have now investigated 27 patients and have been able to draw a clear picture of the necessary plan for examination and treatment. Thyroid neoplasms, according to their degree of differentiation,[6 7] concentrate iodine in the same manner as normal thyroid tissue. In order to discover to what degree they will concentrate iodine it is necessary to give a rather large tracer dose and then either perform a biopsy from which an autoradiogram can be prepared or place a Geiger counter over the lesion. Where normal thyroid tissue is present in the neck it competes so successfully for the isotope that amounts too small to be detected by ordinary counting devices are taken up by the tumour. In addition the carcinoma may have metastasized to areas not far removed from the thyroid and then the intense concentration in the latter may make it impossible to detect the much diminished concentration in the secondary deposits. Because of these difficulties the first step in treating thyroid cancer, especially when it has metastasized, is to excise as much of the primary tumour as possible and all the remaining normal thyroid tissue.[8] This will provide a good biopsy for the pathologist and ensure that normal thyroid tissue is not left to compete with the neoplasm for the radio-iodine. If the patient is unfit or unsuitable for such an operation the normal thyroid tissue can be ablated by means of a therapeutic dose of radioactive iodine. Total thyroidectomy by the knife or by radio-iodine has another important place in this form of therapy. It was first suggested by Means[9] that metastases of a thyroid carcinoma could take over the function of the normal gland, and Rawson[10] was later able to demonstrate that removing all normal thyroid tissue induced a greater uptake of iodine in the remaining tumour tissue in some patients. It is sometimes of help to give these patients either thyrotropic hormone by injection[11] or a course of thiouracil,[12] in the latter case stopping the drug a few days before the therapeutic dose of radio-iodine is given.

In 6 of Pochin's 27 patients it was possible to induce uptake of radio-iodine by the methods outlined above. In an additional four patients some uptake was probable. Such figures are encouraging and show conclusively that earlier workers must have overlooked patients who were potentially suitable for treatment because they had not first destroyed the normal functioning thyroid tissue or because they had not administered a large enough tracer dose. It must be remembered, however, that Pochin's cases probably represent a highly selected series, since it is the differentiated type of tumour which responds best to this therapy and which would naturally be referred to a centre specializing in this work.

Elsewhere in this issue we publish a report from Drs. M. Dargent and P. Guinet, of Lyons, who put forward the suggestion that thyroid carcinoma does not usually arise in a pre-existing adenoma although the two conditions may be incidental fellow-travellers. The genesis of cancer in the thyroid gland has been the subject of much investigation in recent years, especially since Bielschowsky[13] showed that cancer could be produced in the experimental animal's thyroid by giving a goitrogen over a long period supplemented by a carcinogen, in his experiments A.A.F.

[1] Taylor, S., *Postgrad. med. J.*, 1951, **27**, 54.
[2] Rawson, R. W., Rall, J. E., and Peacock, W., *J. clin. Endocr.*, 1951, **11**, 1128.
[3] Dobyns, B. M., and Maloof, F., ibid., 1951, **11**, 1323.
[4] Seidlin, S. M., Marinelli, L. D., and Oshry, E., *J. Amer. med. Ass.*, 1946, **132**, 838.
[5] Pochin, E. E., *Lancet*, 1950, **2**, 84.
[6] Dobyns, B. M., and Lennon, B., *J. clin. Endocr.*, 1948, **8**, 732.
[7] Fitzgerald, P. J., and Foote, F. W., jun., ibid., 1949, **9**, 1153.
[8] Dobyns, B. M., *Surg. Gynec. Obstet.*, 1951, **93**, 415.
[9] *The Thyroid and Its Diseases*, 1937, Philadelphia.
[10] Rawson, R. W., Marinelli, L. D., Skanse, B. M., Trunnel, J., and Fluharty, R. G., *J. clin. Endocr.*, 1948, **8**, 826.
[11] Seidlin, S. M., Oshry, E., and Yalow, A. A., ibid., 1948, **8**, 423.
[12] Trunnel, J. B., Marinelli, L. D., Duffy, B. J., Hill, R., Peacock, W., and Rawson, R. W., ibid., 1949, **9**, 1138.
[13] *Brit. J. exp. Path.*, 1945, **26**, 270.
[14] *Brit. J. Cancer*, 1950, **4**, 223.
[15] Cole, W. H., Slaughter, D. P., and Rossiter, L. J., *J. Amer. med. Ass.*, 1945, **127**, 883.
[16] Crile, G., jun., and Dempsey, W. S., ibid., 1949, **139**, 1247.
[17] Cope, O., Dobyns, B. M., Hamlin, E., and Hopkirk, J., *J. clin. Endocr.*, 1949, **9**, 1012.
[18] Ibid., 1951, **11**, 1281.
[19] Maloof, F., Dobyns, B. M., and Vickery, A. L., *Endocrinology*, 1952, **50**, 612.

(2-acetyl-amino-fluorene). Similarly Doniach[14] has described the induction of malignancy in rat thyroids after the prolonged administration of thiouracil with the addition of a dose of radio-iodine. In the clinical field also there has been some disquiet since the publication of figures from clinics in Chicago,[15] Cleveland,[16] and Boston,[17] indicating that the incidence of malignancy in solitary nodules excised from the thyroid was from 19% to 24.5% and in multinodular goitres 10% to 17.1%. It was inevitable that these two groups of observations should be linked together, though few would agree with Dargent and Guinet when they state, "We think that somehow a previously healthy parenchyma, with or without an old benign adenoma which is the sign of a previous wave of benign hyperplasia, undergoes a special type of hyperplasia when treated with thiourea and carcinogen, or perhaps even with a thiol compound alone. We suggest it should be called malignant hyperplasia." Morris,[18] by an ingenious method of transplantation, produced malignant thyroid tumours in mice after prolonged thiouracil treatment, and those workers who minimize such changes[19] appear to have overlooked the importance of the time factor in this kind of experiment.

REDUCTION OF HOSPITAL STAFFS

During the past year the Ministry of Health has sent teams of medical men to review the staffing of hospitals. These teams have submitted their reports to the Minister, and recently, for example, boards of governors of teaching hospitals have received schedules from the Ministry against which to measure their existing medical staffs, and have been asked to inform the Ministry within three months of what they consider to be the correct establishments. The letter from the Ministry to boards of governors states that when the Minister has approved the establishment of any given hospital the board will be expected to reduce the staff accordingly; and "*it will be permissible for the Board to increase the approved medical establishment in any grade in any specialty only with the Minister's consent in each case.*" [Our italics.]

In this week's *Supplement* Sir Russell Brain draws attention to the fact that one of these letters has, as he puts it, "come to the notice of the Joint Consultants Committee" and that ". . . no opportunity was given to the Committee of discussing with the Ministry the very important implications of the action proposed." This is an excellent example of how not to do things. It may be argued that discussions with the profession's representatives were unnecessary before the issue of these letters since no final decision could be taken until the comments of the boards had been received. But, if the Minister, as we are sure he does, and his officials, as we trust they do, hope for the closest co-operation between those who look after the welfare of the hospitals in the N.H.S., they must take into their complete confidence those who, by the profession's choice, represent the medical men and women who work in the hospitals. These staffing schedules, arriving "out of the blue," will give rise to grave suspicions and uncertainty in the minds of consultants as to the Ministry's intentions. Some control must be exercised over the total consultant establishment, but in a delicate and important matter of this kind the Ministry should have known that consultation with the Joint Committee at the earliest stage of action was essential, and that to wait until the stage of final decision would be most unwise.

It is important to remember that now the State, through the N.H.S., has guaranteed a comprehensive free medical service to the whole population it cannot possibly fulfil the terms of its guarantee unless hospitals are properly equipped and staffed, and unless, too, those working in them feel that they are co-partners in a joint enterprise and not just casual labour to be hired and fired according to the latest ruling from the Treasury. No doubt the hard-pressed officials at the Ministry are having to carry out Treasury instructions; but even in doing this they would do well to secure the co-operation of the medical profession in setting about their appointed task. This task, it would seem, means in many cases reduction of staff. What is to happen to those whose jobs will be thus brought to an end? The boards are obliged, Sir Russell points out, to find them alternative work, but even then, can anyone, least of all those affected, feel happy about the situation which has been allowed to develop? Will the boards be able to find alternative work in the face of an all-round reduction of staffs? It is the answer to these questions which many will want to know, questions which consultation with the profession might have helped to answer in advance. The young and coming generation of consultants must reflect somewhat cynically on the exaggerated promises made by politicians in particular before the Health Service came into operation. There was then foretold in glowing terms the widely opening opportunities for consultants and specialists in the National Health Service. An increase by as much as 50% was foreseen by some well-known apologists. The present incident to which Sir Russell draws attention is yet another illustration of the dangers of centralization. Those who are pressing for decentralization in the administration of the hospital services will be encouraged by this to redouble their efforts.

BONE-MARROW DEPRESSION AND THIOSEMICARBAZONE

Earlier this year we published a letter from Drs. V. U. Lutwyche and D. A. Brewerton[1] describing two cases of bone-marrow depression in patients who had been treated for pulmonary tuberculosis with thiosemicarbazone; and at a recent inquest in London a verdict of death by misadventure was brought in on a woman who died from aplasia of the bone marrow caused by this drug.[2] The thiosemicarbazones were introduced for the treatment of tuberculosis in 1946 by Domagk and his colleagues[3] in Germany, where they were widely prescribed. They were little used elsewhere until 1950, when they were studied in America and in Great Britain. Simmons and his colleagues[4] tried the drug in 16 patients, 11 of whom developed anaemia, dermatitis, or liver disorder; in all the patients cough and expectoration were both lessened. Belgorod and his colleagues[5] reported on its use in 84 patients and concluded that it was effective only when given with streptomycin or P.A.S.; they observed anaemia in 32 and granulocytopenia in 35 of the patients, though recovery occurred spontaneously. Sandhaus and his co-workers[6] treated 14 patients, among whom there was one case of agranulocytosis, two of haemolytic and one of simple anaemia, and four patients had to stop taking the drug because it caused nausea and vomiting; they concluded that there was no reliable evidence of benefit to the patient. Livingstone and Street[7] in Great Britain obtained much more satisfactory results, but out of 45 patients treated by Childress and his colleagues[8] 9 developed dermatitis, 12 fairly severe liver dysfunction, and nearly all of them anaemia. These authors conclude, "It may properly be used for patients who have ceased to improve, or who have worsened, under general supportive treatment and other chemotherapeutic agents." A great many reports on toxicity are to be found in the German literature. The early reports are of damage and death from very high doses, one series having 3 deaths out of 10 patients treated, and another 4 out of 23, when doses as high as 25 mg. per kg. daily (about 1.75 g. daily) were used. Martini and his colleagues[9] recorded some toxic manifestation in 38 out of 72 subjects, and Pribilla and Koester[10] described several cases of severe anaemia. Post-mortem examination of patients who had died while under treatment showed gross fatty degeneration of the liver.[11] It is interesting to note that both in Germany and in the United States the dose has steadily fallen, Staich and his co-workers,[12] who started with up to 4,000 mg. daily, being now content with never more than 200 mg. and usually with 100 mg. daily. In view of all these reports of toxicity it seems doubtful whether thiosemicarbazone should be used except for the patient who fails to improve with other forms of treatment.

Many synthetic chemicals which have recently been introduced are capable of curing some patients but can cause unpleasant or dangerous side-effects in others. For instance, thiouracil,[13] antazoline,[14] "pyribenzamine,"[13] troxidone,[13] methoin,[13] "diparcol,"[15] the sulphonamides,[13] and amidopyrin[16 17] can all cause agranulocytosis; troxidone[13] and allylisopropylacetylurea[13] can cause thrombocytopenia; organic arsenicals,[13] sulphonamides,[13] methoin,[13] and phenylacetylurea[18] can cause marrow aplasia; amphetamine[13] and sulphonamides, especially "promin,"[13] can cause haemolytic anaemia; and cinchophen, phenylacetylurea,[19] and carbon tetrachloride can all cause liver damage. Even the antibiotic chloramphenicol is now known to cause aplastic anaemia.[20 21] All these potentially toxic drugs may be prescribed so freely as to make it impossible to decide which of several actually caused death.[22] Every practitioner must face the possibility that serious toxic effects may be caused by potent drugs, but at present there is no way in which the accumulated experience of the profession can be obtained. Discombe[16] has suggested that a standing committee of clinical and forensic pathologists should be set up to collect the facts. Under the aegis of such a committee a "drug idiosyncrasies registry" could provide valuable information.

1 *British Medical Journal*, 1952, **1**, 1302.
2 *Daily Mail*, November 5, 1952.
3 See leading article in *British Medical Journal*, 1951, **1**, 128.
4 *Amer. Rev. Tuberc.*, 1950, **62**, 128–43.
5 *Dis. Chest*, 1951, **20**, 1–18.
6 *Amer. Rev. Tuberc.*, 1951, **64**, 170–81.
7 *Tubercle (Lond.)*, 1951, **32**, 8–13.
8 *Amer. Rev. Tuberc.*, 1952, **65**, 692–708.
9 *Beitr. Klin. Tuberk.*, 1951, **104**, 515–78.
10 *Dtsch. med. Wschr.*, 1949, **74**, 795–8.
11 *Mschr. Kinderheilk.*, 1949, **97**, 349–56.
12 *Beitr. Klin. Tuberk.*, 1951, **104**, 465–514.
13 Whitby, L., and Britton, C. J. C., *Diseases of Blood*, London, 1950.
14 *Dtsch. med. Wschr.*, 1951, **76**, 897–9.
15 *Med. J. Aust.*, 1950, **37**, 2, 295.
16 Discombe, G., *British Medical Journal*, 1952, **1**, 1270.
17 *Helv. med. Acta*, 1939, **6**, 611–46.
18 *Ann. Intern. Med.*, 1950, **32**, 1224–9.
19 *J. Amer. med. Ass.*, 1951, **147**, 17–21.
20 Hawkins, L. A., and Lederer, H., *British Medical Journal*, 1952, **2**, 423.
21 Wolman, B., *ibid.*, 1952, **2**, 426. See also annotation on p. 434.
22 *Dtsch. med. Wschr.*, 1949, **74**, 161–7.

ARTIFICIAL CIRCULATION

In many centres throughout the world serious attempts are being made to devise a safe and satisfactory artificial circulation by-passing the heart and lungs. A pump designed for this purpose at the Buckston Browne Farm, and tried out experimentally on dogs, was recently exhibited at the Royal College of Surgeons.[1] Many technical problems are gradually being overcome, and it should not be long before cardiac surgery can be undertaken in a dry field. In the U.S.A. Helmsworth and his colleagues have recently described[2] the successful use of their artificial oxygenator-pump applied to a case of anoxic cor pulmonale, whereby approximately one-quarter to one-third of the cardiac output was oxygenated through an extra-corporeal circulation over a period of 10 minutes. The patient had heart failure and was breathless and cyanosed. During the period in which some of the blood was oxygenated artificially breathlessness disappeared, the colour improved, and the arterial oxygen saturation rose from about 43% to 60%. Blood returning from the oxygenator-pump was 90% saturated. Elimination of carbon-dioxide was also improved. The red cells were not damaged by the suctional and compression effects of the pump; clotting was prevented by means of heparin.

1 *British Medical Journal*, 1952, **2**, 887.
2 *J. Amer. med. Ass.*, 1952, **150**, 451.

In the particular form of artificial circulation described by the authors, blood from the inferior vena cava was obtained by means of large catheters inserted through both saphenous veins. After passing through the extra-corporeal circuit, oxygenated blood was returned into the arm veins of the patient. The value of this work lies in the demonstration that artificial oxygenation of blood through an extra-corporeal circuit can be carried out safely in man.

The development of an artificial heart and lungs whereby venous blood is oxygenated and the patient's blood pressure maintained at satisfactory levels would be a boon to the cardiac surgeon. At present, operations on the heart and great vessels include repair of coarctation of the aorta, ligation of patent ductus, the creation of an artificial broncho-pulmonary shunt, mitral valvotomy, pulmonary valvotomy, and infundibular resection. The most common congenital abnormality is atrial septal defect, and attempts to repair this under present conditions have been none too successful. The same may be said of ventricular septal defect. Although mitral valvotomy has proved brilliantly successful in most cases of mitral stenosis, there is a large number of cases of mitral valve disease in which incompetence either is the dominant lesion or is of too great a degree for a simple valve-splitting operation to be effective Current methods of attempting to improve mitral incompetence are unlikely to prove satisfactory. Aortic valvotomy has been performed in several cases of aortic stenosis, both in Britain and abroad, but the mortality rate is high and gross calcification may be difficult to overcome. Successful repair of aortic incompetence has yet to be achieved. In a bloodless field and with rather more time at his disposal, the cardiac surgeon will surely be able to correct all these mechanical defects. Physicians should therefore be encouraged to give some hope to patients seriously embarrassed as a result of such lesions, for if their lives can be preserved long enough by good medical treatment there is a fair chance that cardiac surgery may yet come to their aid.

SOCIAL MEDICINE AT OXFORD

When the Institute of Social Medicine was founded at Oxford in 1942 the Nuffield Provincial Hospitals Trust made a grant of £100,000 to cover the expenses of the Institute for 10 years. The grant has now come to an end, and the Board of the Faculty of Medicine at Oxford has recommended that the study be continued but at a lower level of expenditure, with a reader but without an institute.[1] Evidently the board has had the difficult task of having to decide whether to abandon the institute or to cut down on other more vital projects. In a letter in which he discussed this dilemma Professor A. D. Gardner[2] pointed out that, if Oxford were to ask the University Grants Committee to earmark a grant specially for social medicine, this "would falsely imply that social medicine is of such unique importance to us that we must secure it whatever happens to other subjects." Hard economic facts cannot be ignored, and doubtless the decision of the Board of the Faculty of Medicine was inevitable, but all who have an interest in Medicine in its widest aspects will deplore the passing of the Oxford institute, the establishment of which, with a distinguished clinician at its head, proved an unexpected encouragement to those engaged in public health. Since Professor Ryle's death in 1950 Dr. Alice Stewart has directed the work of the institute and has herself conducted important research on the epidemiology of tuberculosis.

In a foreword to the seventh, and last, report[3] of the committee of the Institute of Social Medicine, Sir Ernest Rock Carling states that there are no grounds for regarding the venture as a failure. The example of Oxford in founding a department of social medicine has now been followed by several other universities, and, though there will be no institute and no professor at Oxford, at least there will be a reader to continue the work. This will be some small comfort to the many medical officers of health who had begun to look to the institute at Oxford for inspiration in their investigations of "the influence of social, genetic, environmental factors on the incidence of human disease and disability," to quote the words used to describe the purposes of the institute. In Dorset, for instance, the institute has helped to plan a survey of old people which will enable the county council to estimate fairly exactly the services they will have to provide in the years to come for the care of the elderly and infirm. Public health workers in their turn have been able to help the institute, for, as the director writes in the report, there is a vast army of people in the field "who are every day seeing, hearing, recording, and storing facts which are of vital importance to social medicine research." Once the help of these people has been enlisted facts can be obtained quickly and cheaply, and "combined surveys," in which outside workers have collaborated with the staff of the institute, have increased in numbers and importance. This type of research, which brings in, among others, medical officers of health, school doctors, health visitors, midwives, factory doctors and officials, medical officers of military boards, and central and local government officials, would certainly have had the full support of Professor Ryle, and it is greatly to be hoped that Dr. Alice Stewart and her colleagues will be able to continue it.

THE URBAN SPRAWL

The Ministry of Housing and Local Government's recently published handbook, *The Density of Residential Areas*, deals at some length and in great detail with the problem of the amount of land required for residential areas, and in particular for the houses they contain. This is a subject of considerable importance, for all whose business takes them to the peripheral suburbs of large industrial towns cannot but be alarmed by the amount of land which is being absorbed by building developments. Their alarm can only be exacerbated by the fact that the process appears to be extending itself into an almost infinite future as the cores of the

1 *Oxford University Gazette*, October 9, 1952.
2 *British Medical Journal*, 1951, 1, 473.
3 *Seventh Report* 1951–2, published by the Institute of Social Medicine, Oxford, 1952.

larger towns are allowed to fall into decay, and the inhabitants, in the inelegant language of the planners, are perforce "decanted" into newly developed areas in the suburbs or perhaps into one of the New Towns. Whichever alternative is adopted, the result is the same, for if overcrowding is to be relieved in central areas, marred by blitz and blight, more houses must be built elsewhere, and much land—sometimes fertile agricultural land—is being swallowed up in this way.

The Ministry's handbook might be expected, therefore, to tell us whether the time has come to call a halt to this process, and what possibilities there are of doing so without crippling the Government's housing policy. But unfortunately the result is somewhat inconclusive, even after a long discussion of such technical subjects as occupancy rates, "permissible height indicators," and land costs. The sorry truth is that substantial savings in land can be achieved only by building flats, but the cost of building them is so great that, if this expedient is adopted, rehousing schemes will become much more expensive than they are at present. This remains so even if a density as high as 200 rooms per acre is adopted. The only encouraging thing that the Ministry's planners find themselves able to say is that "it may be possible to attain a saving of about 20% [in the use of land] compared with pre-war practice at no greater cost, by a modest increase in net density involving freer use of terraces and low flats."

Many of us will feel a keen sense of disappointment that so poor a mouse has issued forth from such a mountain of words and so loud a thunder of argument. The planners should surely be asked to think again and to question their assumptions with greater care. Although the handbook is primarily a technical publication, no attempt is made to show how much could be saved if *more* land were used and *fewer* flats were built; it is implied too readily that the use of land for houses is a "bad thing" in itself. There is much to be said for conducting an economic survey to discover to what extent the use of agricultural land for this purpose really does involve a net economic loss, when all the relevant factors, such as suburban gardening, have been taken into consideration. It is stated in the handbook that development at low densities has often destroyed "social cohesion." This provides a clue which should be followed up. The real problem of the planner may be found to lie in the need to discover ways of preventing this from happening. It may, indeed, even be demonstrated on further inquiry that densities as high as 20 houses or 100 rooms to the acre are possible of attainment without constructing any flats at all, and without sacrificing social amenities to any substantial degree, if more careful attention is directed to the problem of layout.

POLIOMYELITIS AND TONSILLECTOMY

The risks of infection from cases of acute poliomyelitis have been much in the minds of those who have opposed moving the Metropolitan Ear, Nose, and Throat Hospital to the Western (Fever) Hospital, Fulham. The Minister of Health has now asked the South-west Metropolitan Regional Hospital Board to postpone the move, so that the dangers of cross-infection may be further considered.[1] Whatever they may be in those particular circumstances, there are certainly reasons for believing that tonsillectomy may precipitate or aggravate an attack of poliomyelitis. However, the effect of recent or old tonsillectomy on the total incidence of poliomyelitis has been a matter of debate, and contradictory conclusions have been drawn. Further contributions to the knowledge of these problems have now come from the U.S.A.

Dr. A. H. Miller,[2] analysing the cases of poliomyelitis in Los Angeles City and Los Angeles County, shows that the incidence of poliomyelitis did not differ significantly between persons who had had tonsillectomy and those who had not. The prognosis appeared to be poor when a patient had tonsillectomy less than a month before developing poliomyelitis. The percentage of patients who had a recent tonsillectomy and developed bulbar type of poliomyelitis varied from 28.5 to 75 during 1949–51, compared with 15 to 18.5 for all patients. The total number of patients with recent tonsillectomies was only 20, so that undue emphasis cannot be placed on this finding.

Dr. F. H. Top[3] examined the records of 1,947 poliomyelitis patients admitted to the Herman Kiefer Hospital during 1940–9. The percentage of patients with tonsils removed was, for each type of poliomyelitis, 46 for non-paralytic, 43 for spinal, 85 for bulbar, 69 for spinobulbar, and 44 for encephalitis. Of the 122 deaths, 38% were due to bulbar and 53% to spinobulbar type of the disease; 93.5% of the bulbar and 56.9% of the spinobulbar deaths had a history of tonsillectomy. Of the patients who had had tonsillectomy within a month of developing poliomyelitis, 57% contracted the bulbar and spinobulbar type, compared with 33.5% for all patients with tonsillectomy. Unfortunately the proportion of tonsillectomized children in the general population was not known, so that the effects of tonsillectomy on the level of the general incidence of poliomyelitis is speculative. Dr. J. L. Wilson,[4] in a discussion of this problem, quotes the findings of other workers. In an inquiry into the epidemic in Utah in 1943 the incidence of poliomyelitis is given as 2½ times as great among tonsillectomized children as in the general child population and the incidence of bulbar cases as 16 times as great.

From the data in the first two studies it appears that the incidence of poliomyelitis is approximately the same in children who have and have not had tonsillectomy. If the operation was carried out less than one month before the attack of poliomyelitis, then the chance that the patient develops the bulbar types and of being more critically ill is increased. The number of patients who had tonsillectomy in the month preceding the attack of poliomyelitis was small and did not affect to any extent the overall incidence of poliomyelitis in the Los Angeles data.

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[1] See *Journal*, p. 1161.
[2] *J. Amer. med. Ass.*, 1952, **150**, 532.
[3] Ibid., 1952, **150**, 534.
[4] Ibid., 1952, **150**, 539.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

ABDOMINAL HERNIA IN CHILDHOOD

BY

DENIS BROWNE, M.B., F.R.C.S.

Surgeon to the Hospital for Sick Children, Great Ormond Street, London

This article deals with the principal herniae of the abdominal contents in children—umbilical, epigastric, inguinal, femoral, and diaphragmatic—as well as with those conditions associated with these herniae or which may cause difficulty in diagnosis.

True Umbilical Hernia

In true umbilical hernia the protrusion comes right through the centre of the umbilical scar. It is possible to feel round the neck of the hernia a collar of fibrous tissue continuous with the linea alba, running distally and finally thinning out over the end of the sac. Herniae of this kind have an invariable tendency to spontaneous cure, owing to the contraction of the fibrous tissue round the neck of the sac, which should normally have occurred at birth but in these cases is merely delayed. Cure can be hindered by a not uncommon vicious circle in which the child forces out the hernia by crying, and so causes pain which makes it cry all the more. On the other hand, it can be accelerated by preventing the protrusion by means of a 3-in. (7.6-cm.) wide strip of zinc oxide adhesive strapping applied transversely in such a way as to bring over the hernial orifice a vertical fold of skin. The plaster will remain in place for about a fortnight if it is kept dry, and the less often it is changed the better. Variations of this simple and effective method, all less efficient, are: (1) the use of pads, coins, etc., under the plaster; (2) the use of extensible plaster instead of the ordinary inextensible type—this is very common, in spite of its obvious unsuitability; and (3), least effective and most expensive of all, the use of rubber belts and various types of corset.

I do not think that operation is ever necessary for this form of hernia, though it is often performed. There is no need for anxiety if a small bulge persists for several years; I have been unable to find any record of a case in which strangulation of bowel occurred. This is curious in view of the notorious tendency to strangulation of umbilical herniae in the elderly. There is one type of operation against which I would offer a particular warning, that of subcutaneous ligature. It is effective only in cases with a strong fibrous collar round the neck of the sac, and these, as has been stated, cure themselves spontaneously; with the "semi-umbilical" types, considered below, it is most disappointing. Apart from this I know of two cases of death from peritonitis as a result of this technique, although I have been unable to ascertain the exact mechanism of the disaster.

Semi-umbilical Hernia

This is the term I use for a hernia in which the sac does not emerge through the centre of the umbilical scar, but through its upper border, in such a way that half of the resultant bulge is covered by the umbilicus and half by the abdominal skin above it. There is no collar of fibrous tissue to be felt around the neck, and the margins of the opening in the abdominal wall are thin. This hernia resembles the true umbilical type in its harmlessness to life, but does not share its tendency to spontaneous cure. Unless closed by operation, the opening persists indefinitely. The bulge can be controlled by the same strapping as is used for the true umbilical type, but later on must be closed surgically. A suitable time for this is about 3 years of age. A short transverse incision is made immediately above the bulge, and through it the neck of the sac is isolated while intact. Then the neck of the sac is severed, and while the skin and distal portion of it are lifted away by means of a self-retaining retractor the resulting gap in the linea alba is closed by two layers of non-absorbable sutures. I have never found any need for more elaborate measures of closure. It may be noted that operations on the umbilicus in children may cause a surprising amount of shock for what is apparently a trivial proceeding; often far more than is produced by opening the chest. Presumably this is because this area is a centre for referred pain impulses.

Exomphalos

The treatment of the severer degrees of exomphalos is outside the scope of this article. There is, however, a minor degree of this alarming deformity the treatment of which is relatively easy; it is that in which the abdominal contents protrude into the umbilical cord but can be milked back into the abdomen without difficulty. Here it is necessary only to twist the cord so as to force the bowel back and narrow the opening in the abdominal wall, and then to maintain this position by firmly applied strapping. This is left on for a fortnight, in spite of any protests that may be made that the dressing needs changing because there is a discharge under it. When it is removed it will be seen that the natural processes of obliteration of the umbilical opening have taken place in a surprising way, and that the abdominal wall looks normal.

Other Umbilical Abnormalities

Umbilical Polyp.—This is a small island of intestinal mucosa shut off on the outside of the abdomen by the closure of the umbilical orifice. It causes a persistent mucous discharge, and shows as a moist red protuberance in the centre of the umbilicus. Repeated applications of silver nitrate, or a single application of diathermy or cautery, will destroy the mucosa and end the nuisance.

Meckel's diverticulum may present as a fistula at the umbilicus through which a probe can be passed into the bowel. Laparotomy is the only treatment.

Patent urachus is an excessively rare condition in which the bladder has an opening at the umbilicus. Treatment is obvious and not particularly difficult.

Pubic Umbilicus.—Occasionally the umbilicus is situated just above the pubic symphysis, so that the bladder lies directly under it. This is merely an oddity for which no treatment is necessary.

Epigastric Hernia

These herniae are small protrusions of the fatty extraperitoneal tissue through minute openings in the linea alba above the umbilicus. Apparently they never occur below. They are usually so small as to be difficult to see through the skin, unless there is a good side-light. They do not contain peritoneal sacs and are in no way dangerous, but they may become painful, apparently because of partial strangula-

tion of the neck of the protrusion. If this occurs they should be exposed through a small transverse incision and removed after ligating the neck. The small orifice in the linea alba can be closed by a single non-absorbable stitch.

Inguinal Hernia

With a more rational system than we have at present of collecting and arranging medical knowledge it would be possible to discard such absurdities as the description of one particular variety of the failure of obliteration of the processus vaginalis as "infantile hernia." The work of Hamilton Russell showed that all inguinal herniae in children are congenital deformities, and they might be divided into the "complete," in which the entire processus vaginalis persists so that the bowel in its descent actually impinges on the testis, and the "incomplete," in which the tunica vaginalis is shut off from the hernial sac. There is no great importance in this division, as in symptoms, prognosis, and treatment the two kinds are exactly the same.

Unless bowel is actually present in the sac it may be impossible to decide by examination whether a hernia is present or not. However, the characteristic history of a lump that comes and goes in the inguinal region, appearing particularly after straining or at the end of an active day, is enough to establish the diagnosis, as no other condition gives such signs.

In certain cases a truss is very useful, either as a method of cure or to tide an infant over a period when operation is inadvisable. If a small hernia appears soon after birth and an efficient truss is applied without delay there is no doubt that permanent cure can be obtained in many cases. In most cases, however, the main use of a truss is to avoid, as everyone of experience prefers to do, operations upon infants during the milk-feeding period.

I think there is only one form of truss which is satisfactory—the horseshoe-shaped solid rubber one. Skeins of wool, one-sided trusses, and pneumatic pads are all inefficient compared with this. The truss should never be removed, but simply lifted to allow cleaning the skin below it, and with the necessary renewals should be kept on throughout the first year. It can then be taken off and events observed. If the hernia appears there is now no chance of cure by this means, and operation should be advised. If it does not, a guarded prognosis should be given, as it is never possible to be sure whether the sac is obliterated or merely empty.

Once the child is over the first year, operation without undue delay is the only treatment, since the more the bowel descends the more the orifice is stretched, and there is always the risk of the protrusion becoming jammed.

The incision should be made transversely, curved slightly in the lines of the folds of the skin, just above the pubic symphysis, and should be long enough to expose both external rings. If a double hernia is present it is much the quickest to treat both sacs through a single incision; in the case of a single hernia exploration of the other side will reveal a sac that hitherto has given no signs in about 20% of cases. A last and not entirely negligible advantage of this incision is that no one who uses it can possibly operate upon the wrong side. This incision heals extremely well and, unlike the classical one in the line of the inguinal canal, is in adult life entirely hidden by the pubic hair.

The trick of easy dissection of the hernial sac turns upon grasping the testicle in a tough but unimportant part by an artery forceps, and holding it out of the wound so as to put the cord upon the stretch. This can be done without disturbing in the slightest its relations in the scrotum. Then with blunt dissecting forceps the sac is delicately extracted from the spermatic cord and ligated under strong tension by a transfixing suture of unabsorbable material. If this is done properly the closed neck, when released by cutting off the sac below, should shoot upwards to well above the internal ring. If the external ring is much stretched it should be narrowed by a couple of sutures; otherwise the testicle should be returned to the scrotum and the incision sutured, care being taken that the testicle is not caught up by an incautious stitch and anchored in the wound.

Hernia with Undescended Testicle

In this case the inguinal canal must be opened and the internal ring freely exposed. For this purpose a frame retractor of the type I use, which will pull any structure in any direction and in any plane, will be found a great help. As in the simple herniae, the keeping of all the structures upon the stretch is the secret of any easy dissection, and for this purpose the testicle should be extracted from the sac and grasped discreetly by artery forceps as a first step in disentangling the structures of the cord. The sac is the tightest of all the structures which oppose the descent of the testicle, and once it is divided the only other permissible freeing consists in the isolation and division of its suspensory fibres. These, undescribed by anatomists but easily demonstrated, run from the back wall of the abdomen in a fan-shaped layer into the outer edge of the cord.

The best way of fastening down the testicle is to make a special tunnel for it underneath the narrow passage which connects the upper and lower scrotal cavities. Tough fixed fibrous tissue lies in front of the pubis at this point, and once the testicle is dragged through this by means of an artery forceps thrust up through a small incision in the scrotum it lies firmly fixed but free from stimulus in the upper part of the scrotum. Atrophy of the testicle after operation to correct its position is far more frequent than would be gathered from reading works upon the subject, and I think the main cause of this atrophy is venous engorgement due to spasm of the veins. At any rate pronounced swelling of the testicle after operation is a most sinister sign and usually foretells the disappearance of the gland. It can be guarded against by leaving the veins unstimulated by any drag upon them after operation, and by incising the tunica albuginea of the testicle to allow free escape of oedema before pulling it down.

I dislike all forms of fixation, such as Bevan's and more particularly Torek's, that put a strain on the long leash of testicular vessels which no one would dare to inflict upon the very similar blood supply of a caterpillar skin flap.

Jammed, Irreducible, or Strangulated Hernia

I have never seen a hernia in a child which was irreducible, provided that the following trick of reduction was employed. It consists in using the fingers of one hand to form a kind of funnel leading into the external ring, while those of the other hand grasp the lower end of the sac. Then by alternate squeezing and releasing of the grip of each hand a pulsating to-and-fro movement of the contents, which are mainly fluid, is set up and maintained until they can be felt to escape back into the abdomen; at first drop by drop of contents, and then actual loops of bowel. After reduction operation should be performed without delay.

There are certain contraindications to trying this method of reduction when it might result in returning to the abdomen either gangrenous bowel or a necrotic testicle. I have seen it stated that strangulation and gangrene of the bowel do not occur in the inguinal herniae of children. This is incorrect and a most dangerous teaching. I have known several deaths from this cause, one occurring from a small Richter hernia in an infant under the charge of a very experienced surgeon; and on two occasions I have had to resect gangrenous bowel extracted through an internal ring enlarged by an outward cut through the surrounding muscles.

The danger signs which indicate immediate exploration of the area rather than taxis are: (*a*) if a child with symptoms of intestinal obstruction shows any tenderness or

thickening in the region of the external ring; (*b*) if vomiting of the obstructive type is present; and (*c*) if there is any redness or oedema of the skin over a hernial bulge.

In operation upon such cases the surgeon must be prepared for all kinds of curious conditions, including not uncommonly the death of the testicle. This is due to obstruction of the latter's very vulnerable blood supply, either by torsion of the mesentery of the testicle or by compression of the artery at the external ring. In one curious case the testicle was gangrenous because a piece of omentum strangulated in a minute hernial sac had secreted enough fluid to expand the neck of the sac and compress the testicular artery. In the female a not uncommon content of the sac of an inguinal hernia is the ovary, apparently trying to follow the path of the male gonad, and feeling to the examining finger extremely like an inguinal ectopic testicle. In such cases operation should not be delayed, as partial strangulation is quite common, and is followed by dense adhesions which make reposition of the organ very difficult.

Torsion of the Testicle

I consider there are two different conditions, with different prognoses and for which different treatment is necessary, which are usually lumped together under this heading.

Torsion of the Cord of the Testicle.—In this condition the gland, complete with its covering of tunica vaginalis, is rotated as a whole inside the scrotum. The onset is often not very acute, and the twist may spontaneously undo itself, to recur with greater or less severity. The treatment is a gentle rotation of the testicle, finding the correct direction in which to do this by noting whether the first way in which it is twisted increases or diminishes the symptoms. As a prophylactic measure I have sewn the tunica vaginalis of both testicles together through a small incision in the scrotum.

Torsion of the Mesentery of the Testicle.—In this condition the onset is usually abrupt and extremely painful. If operation were performed without any delay at all most of the organs could probably be saved, but I have never known this to be prompt enough. It is particularly apt to occur in maldescended testicles in hernial sacs, and I have known one death occur through an error of judgment which led to the preserving of a necrotic testicle and the consequent infection of the peritoneal cavity.

Types of Hydrocele

Fluid Inguinal Hernia or Communicating Hydrocele.—This is really a "complete inguinal hernia" in which the part of the sac formed from the processus vaginalis has so nearly approached its normal obliteration that it remains merely as a tube of peritoneum so narrow that it will permit only the passage of fluid from the abdomen into the serous space round the testis. The distinguishing point from a true hydrocele is that the collection of fluid into the tunica vaginalis varies in size according to whether the patient has been lying in bed or running about. The treatment is operation, as otherwise the condition will persist indefinitely, unlike an ordinary hydrocele.

Hydrocele of the Tunica Vaginalis.—For some unknown reason fluid is apt to accumulate round the testicle in some children, particularly during the first two years of life. This collection is in no way dangerous, and will almost invariably disappear in the course of a year or two as mysteriously as it came. In a few cases the tunica may become so tense as to cause discomfort, and then it may be exposed through the incision recommended for hernia, opened, and everted. Simple tapping of the fluid is quite futile and seems, if anything, to delay its disappearance; I have no experience of the injection of irritants that is sometimes recommended, but the disadvantages of this for such a harmless condition seem obvious.

Hydrocele of the Cord.—This is an accumulation of fluid in an unobliterated but isolated portion of the processus vaginalis. It has very little tendency to spontaneous absorption, and usually an operation is necessary to remove the sac it lies in.

Femoral Hernia

Though rare, this condition does occur in children. Its pathology is puzzling, as there is a narrow sac surrounded invariably by a kind of lipoma continuous with the extraperitoneal fat. This fatty collection can usually be felt quite plainly, even when the sac is empty. I have found Lothiesen's approach to the neck of the sac through the inguinal canal very satisfactory, though it is often necessary to dissect away the fat in order to withdraw the sac through the femoral canal. The incision is the same as for an inguinal hernia, and the femoral canal is closed with an unabsorbable stitch.

Diaphragmatic Hernia

The possibility of this condition should always occur to anyone faced with a baby or older child suffering from attacks of interference with the proper working of the bowels or lungs, or both together. Once it is diagnosed, even if in the first few days of life, immediate operation is far safer than delay. The jamming of the contents of a diaphragmatic hernia is always a danger, and when it occurs is of a peculiar deadliness, both on account of the large amount of bowel usually involved and because of the pressure on the heart exerted by the gaseous distension of its obstructed loops. An approach through the chest is far safer and easier than that through the abdomen. Also—and this is very important—it requires much less anaesthetic.

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SUPPLEMENTARY LIST OF APPROVED NAMES

The Pharmacopoeia Commission has issued the following Supplementary List of Approved Names:

AZAMETHONIUM BROMIDE (3-methyl-3-azapentane-1:5-bis(ethyldimethylammonium) dibromide, "pendiomide"); BENZYLALKONIUM CHLORIDE (alkylbenzyldimethylammonium chloride, "zephiran chloride"); CARAMIPHEN (2-diethylaminoethyl 1-phenyl*cyclo*pentane-1-carboxylic acid, "parpanit" is the hydrochloride); CHLOROPYRILENE (*N*-5-chloro-2-thienylmethyl-*N'N'*-dimethyl-*N*-2-pyridylethylenediamine); CHLOROQUINE (7-chloro-4-(4-diethylamino-1-methylbutylamino)quinoline, "aralen"); CO-CARBOXYLASE (pyrophosphoric ester of aneurine); DEXTRAN; DICHLOROPHENARSINE (3-amino-4-hydroxyphenyldichloroarsine); DISULFIRAM (tetraethylthiuram disulphide, "antabuse"); DOXYLAMINE (2-(α-2-dimethylaminoethoxy-α-methylbenzyl)pyridine, "decapryn"); EUCATROPINE (4-mandeloyloxy-1:2:2:6-tetramethylpiperidine "euphthalmine"); GENTISIC ACID (2:5-dihydroxybenzoic acid); GLUTAMIC ACID (1-aminopropane-1:3-dicarboxylic acid); HYDRALAZINE (1-hydrazinophthalazine, "apresoline" is the hydrochloride); HYDROXAMETHOCAINE (2-dimethylaminoethyl 4-*n*-butylaminosalicylate); MERALLURIDE (mixture of *N*-(3-hydroxymercuri-2-methoxypropylcarbamyl)succinamic acid and theophylline, "mercuhydrin"); MERCAPTOMERIN SODIUM (disodium salt of *N*-(3 carboxymethylthiomercuri-2-methoxypropyl)camphoramic acid, "thiomerin sodium"); MERCUROPHYLLINE SODIUM (mixture of the sodium salt of *N*-(3-hydroxymercuri-2-methoxypropyl)camphoramic acid and theophylline, "mercuzanthin"); METHANTHELINIUM BROMIDE (2-diethylaminoethyl xanthen-9-carboxylate methobromide, "banthine bromide"); METHAPHENILENE (*N'N'*-dimethyl-*N*-phenyl-*N*-(2-thienylmethyl)-ethylenediamine, "diatrin" is the hydrochloride); METHIODAL SODIUM (sodium iodomethanesulphonate, "skiodan sodium"); METHOESTROL (αβ-diethyl-4:4'-dihydroxy-3:3'-dimethylstilbene); METHYLERGOMETRINE ((+)-1-hydroxy-2-butylamide of (+)-lysergic acid, "methergin" is the tartrate); NEOCINCHOPHEN (ethyl 6-methyl-2-phenylquinoline-4-carboxylate); OXYPHENONIUM BROMIDE (2-diethylaminoethyl α-*cyclo*hexyl-α-phenylglycollate methobromide, "antrenyl"); PENT-

AQUINE (6-methoxy-8-(5-*iso*propylaminoamylamino)quinoline); PHENTOLAMINE (2-*N*-*m*-hydroxyphenyl-*p*-toluidinomethyliminazoline, "rogitine" is the hydrochloride); PHENYLBUTAZONE (4-*n*-butyl-1:2-diphenylpyrazolidine-3:5-dione, "butazolidin"); PIPEROCAINE (3-(2-methylpiperidino)propyl benzoate, metycaine is the hydrochloride); POLYVIDONE (polyvinylpyrrolidone); PREGNENOLONE (3-hydroxy-5-pregnen-20-one); PROPYLIODONE (*n*-propyl 3:5-di-iodo-4-pyridone-*N*-acetate); SODIUM CYCLAMATE (sodium *cyclo*hexylsulphamate, "sucaryl"); SULPHAMETHIZOLE (2-*p*-aminobenzenesulphonamido-5-methyl-1:3:4-thiadiazole, "urolucosil"); SUXAMETHONIUM CHLORIDE (bis-2-dimethylaminoethyl succinate bismethochloride, "scoline"); SUXETHONIUM CHLORIDE (bis-2-dimethylaminoethyl succinate bisethochloride); THONZYLAMINE (*N*-*p*-methoxybenzyl-*N'N'*-dimethyl-*N*-2-pyrimidylethylenediamine, "neohetramine"); VINBARBITONE (5-ethyl-5-(1-methylbut-1-enyl)-barbituric acid, "delvinal").

The Approved Names amidone and isoamidone are withdrawn, and replaced as follows: METHADONE (6-dimethylamino-4:4-diphenylheptan 3-one, amidone, "physeptone" is the hydrochloride); ISOMETHADONE (6-dimethylamino-5-methyl-4:4-diphenylhexan-3-one, isoamidone).

Nova et Vetera

ALMROTH WRIGHT

Bibliography of the Published Writings of Sir Almroth E. Wright, M.D., F.R.S. Compiled by Leonard Colebrook, F.R.S. (Pp. 32. Price 6s.) London: William Heinemann (Medical Books) Ltd. 1952.

Dr. Colebrook is a very distinguished pupil of a great master. The preparation of this bibliography must have been a laborious task and is clearly an act of piety. As such it should be treated with piety. He has adopted the admirable and self-sacrificing method of attaching to each entry a brief statement of what it contains and, in some cases, an explanation of the circumstances under which it was written. Dr. Colebrook does not state whether his list of the writings of Almroth Wright is complete, but he does include 144 entries and just one-twelfth of that number of separate volumes. We suspect that he could have greatly increased the number of entries, for Wright wrote quickly and easily, and he obviously enjoyed writing. So combative a man who lived to be 80 may well have written far more. In exercising some selection Dr. Colebrook has, we think, done wisely. It is among the terrors of advancing years that one's earlier and rasher pronouncements may be made public, for if iniquities were counted which of us would stand? We may therefore assume that Dr. Colebrook has, quite rightly, prepared such a bibliography of Wright as Wright would have wished. Perhaps a selection of the selection—the titles of a few of his books—will suffice to give those who do not remember Wright some idea of his wide range of interests:

1904: *A Short Treatise on Antityphoid Inoculation.* 1909: *Studies on Immunization.* 1913: *The Unexpurgated Case against Woman Suffrage.* 1941: *Prolegomena to the Logic which Searches for the Truth.* 1942: *Pathology and Treatment of War Wounds.*

Looking back, *longo intervallo*, on this great man's life, one may ask what were his main achievements? His many positive contributions to scientific medicine would alone sustain his memory, but they, after all, will in the end be replaced, and the reviewer would like to put his claims on our memory and gratitude higher yet than one among many able and original investigators. First, Wright drew the attention of all scientific workers to the extreme importance of technique. Secondly, he convinced all involved in medicine as science that it is the living body itself that must recover and that it cannot be treated as a test-tube into which chemicals can be poured. Thirdly, his influence was most important in convincing the effective British public that it was essential for national health and safety that scientific research should be adequately supported. All these factors have been significant for the advances that, during the last 20 years, have led to the prolongation of human life. For that Wright was largely responsible. How he did it the reader may learn by perusing the titles in this bibliography and Dr. Colebrook's discerning notes on them.

CHARLES SINGER.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Growth of Children

SIR,—A recent annotation in the *Journal* (October 25, p. 930) drew attention to the publication by Aberdeen University Court of the records of the measurements of children from birth to 5 years of age made some 20 years ago by the late Professor Low.[1] It is perhaps a pity that his colleagues who have compiled this invaluable collection of tables from Professor Low's record cards should have gratuitously stated in their foreword some of Professor Low's opinions. "Professor Low," they say, "profoundly disagreed with the current statement that children of to-day are taller and heavier (than formerly); he maintained that, however excellent the nutrition received by certain children, they would not grow beyond the size of their type, and he was convinced that, even if food was poor, provided a child got sufficient it would reach the stature for its particular stock." It is more than a pity that the writer of the annotation, having stated the above quotation, should then go on: "When we reflect that this serious statement was made by one who at least had gathered the facts we may in turn have serious reflections on public expenditure and political claims made on inadequate data."

Professor Low had gathered facts—over 20,000 measurements of 126 children—but he had not gathered *the facts relevant to the statement.* He was, of course, entitled to have and to state his convictions on what influences or does not influence growth, but he has not produced any facts in support of them. On the other hand, there is no shadow of doubt that children of to-day during the period of active growth are taller and heavier than formerly. This secular change in growth is well established. For example, in some 40 years to 1949, the average height of London schoolboys increased by 2.9 in. (7.5 cm.) and the average weight by 9 lb. (4.1 kg.).[2,3] Between 1924 and 1951 the average height of Glasgow boys of 13 years increased by 4.4 in. (11.2 cm.) and the average weight by 14.9 lb. (6.8 kg.).[4] When the latest available data for Aberdeen are compared with Professor Low's figures for the period 1928–32 they indicate an increase at age 5 years of 1 in. (2.6 cm.) in height and 3.3 lb. (1.5 kg.) in weight. At the same time it should be pointed out that to regard the secular change in growth merely as an increase in height and weight is misleading. It is much better to regard it as accelerated growth.[5] Children of to-day are growing faster, at least 15% faster than those of 40 years ago, but the final height attained has not increased proportionately, and indeed it is not yet settled whether there is any increase at all.

We may or may not have serious reflections on public expenditure and political claims made on inadequate data, but it reflects no credit on the *Journal* to use the prestige of Professor Low as an anthropologist to misguide the reader as to the effects of diet and heredity on the growth of children.—I am, etc.,

Glasgow. JOHN B. DE V. WEIR.

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1 *Growth of Children: 66 Boys and 60 Girls Each Measured at Three Days and at One, Two, Three, Four, and Five Years of Age.* University of Aberdeen. 1952.

2 Menzies, F. (1940). *Report by the School Medical Officer on the Average Heights and Weights of Elementary School Children in the County of London in 1938.* London County Council.

3 Daley, A. (1950). *Report on the Heights and Weights of School Pupils in the County of London in 1949.* London County Council.

4 Ewan, J. (1952). *Report on the Medical Inspection and Treatment of School Children,* Glasgow Education Health Service, Public Health Department, Corporation of Glasgow.

5 Weir, J. B. de V. (1952). *Brit. J. Nutr.* 6, 19.

SIR,—Your annotator (October 25, p. 930) quotes the late Professor Alexander Low as disagreeing profoundly "with the current statement that children of to-day are taller and heavier than formerly." He goes on to say: "When we reflect that this serious statement was made by one who at least had gathered the facts we may in turn have serious reflections on public expenditure and political claims made on inadequate data." In consequence, the Press on Sunday, November 2, carried sensational headlines suggesting to the lay public that a national policy aimed at a high standard of nutrition is a waste of money. It would be a great pity if this sort of dangerously ignorant nonsense prevented us from consolidating and extending the nutritional gains acquired with much effort and with incalculable benefit to health over the past 15 years.

Your annotator has gone astray on two counts. Professor Low's opinion was given in the introduction to the Aberdeen report presumably as a piece of curious information about an eminent man, and is not a conclusion based on the figures presented in the main report. These figures cannot be used either in support or in rebuttal, and I am fairly sure that Professor Low did not possess any other information which is more relevant. Secondly, how many who have studied the literature would agree that the evidence in favour of children being taller and heavier nowadays is "inadequate"? Professor Low was probably not aware of recent and convincing evidence (Weir, J. B. de V., *Brit. J. Nutr.*, 1952, **6**, 19) before his death; but your annotator would not be able to justify himself by pleading ignorance.

It might undo some of the damage if you now publish another annotation based on a careful and scientific appraisal of the evidence.—I am, etc.,

London, S.W.5. ANGUS M. THOMSON.

Post-epileptic Automatism

SIR,—Some time ago I gave evidence in a murder case in which an epileptic had strangled his landlady. The prosecution argued that this could not have been a case of post-epileptic automatism, since in that condition the epileptic tended to perform some habitual or automatic action. The example was quoted from East's *Introduction to Forensic Psychiatry in the Criminal Courts* of a woman cutting bread-and-butter and having a fit; she injured her children with the knife. It was suggested that a person wringing out clothes might strangle in an automatism, but the epileptic would not strangle *ab initio*.

It is by no means easy to determine whether this is so, since cases of automatism are rare and difficult to observe even in institutions. However, with the advent of convulsive therapy it is easy to see post-epileptic behaviour, and in my experience such observations are entirely contrary to East's views. I can remember a number of cases of such post-epileptic automatism which I have had an opportunity of seeing, and they seem controlled by the mental content rather than habitual actions. I have never seen a shoemaker automatically hammering an imaginary shoe, a tailor sewing an imaginary coat, and so on. One case which shows the importance of the mental content was that of a woman who had been for some time the mistress of a very rich man. He had finally discarded her, and she became depressed. She was treated in the days when fits were evoked by leptazol. After a fit she tried to embrace everyone in the neighbourhood, although, of course, unconscious of her behaviour. Another, a man, after E.C.T. always tried to find a cross which he said he had had round his neck, although actually he had not worn it. He was an ardent Catholic and very religious. It is easy to remember similar cases.

It would be very interesting to know the opinion of other psychiatrists on this matter, since obviously it is of great medico-legal importance, and erroneous ideas still persist in the textbooks.—I am, etc.,

London, W.1. CLIFFORD ALLEN.

Umbilical Hernia

SIR,—Advertisements have appeared which suggest that supporting belts may be needed in the "pre-operative management of umbilical hernia in childhood," and it was stated that these herniae cause constipation and abdominal discomfort. The general principles underlying the natural history and subsequent progress of infants affected with umbilical hernia have been carefully studied over the past several years, and, arising out of this experience, I submit the following comments.

1. In well over 200 cases of umbilical herniae in children that I have personally observed, in all but a very few cases the mother emphatically declared that the hernia was causing no symptoms. I have never known an umbilical hernia cause constipation and cannot see any anatomical reason why it should. On the other hand, umbilical herniae tend to persist after the period of infancy in flabby children as opposed to firm healthy children; and it is also this type of child who may suffer from constipation. I have been unable to find a record of a case of strangulation of an infantile umbilical hernia.

2. Any type of support which tends to restrict muscular activity will accentuate the condition of flabbiness rather than cure it. Good diet, vitamins, fresh air, and healthy muscular movement are more likely to cure the hernia than any restricting support.

3. There is no justification for the idea that bringing the recti muscles into apposition will cure the umbilical hernia:

(*a*) A child may have wide divarification of the recti muscles with no umbilical hernia.

(*b*) A child may have wide divarification of the recti and a hernia; and the hernia may cure itself while the recti are still widely divarificant.

(*c*) The recti muscles play no part in the formation of the umbilical ring through which the hernial sac protrudes. The ring is entirely fascial, composed of a condensation of fibres from the linea alba reinforced by fibres from the ligaments produced by the obliterated umbilical vein, umbilical arteries, and urachus. The medial edges of the recti muscles run alongside the ring, and the muscles are connected to the linea alba only by the tendinous insertions of the rectus muscle into the rectus sheath. One of these insertions always occurs at the level of the umbilicus. There is some anatomical evidence that a layer of fascia—the umbilical fascia—develops during infancy between the linea alba and the peritoneum and closes over the umbilical orifice. Thus to bring about a cure of an infantile umbilical hernia there must be some strengthening and growth of fascia. Fascia is said to be inert and to increase in strength when exposed to muscular stress.

My belief is that the rupture is cured by the normal muscular activity of a healthy child, and any appliance which restricts muscular movement tends to prevent the natural cure of the hernia.

4. The tendency to spontaneous cure is very great, and, although a very small percentage may require surgery, the child should be given a period of several years before operation without any appliance to see if the hernia will cure itself in cases where previously an appliance has been worn.

But as a rule for all cases of umbilical hernia I would advocate no appliance, belt, strapping, or binder, but reliance on healthy living and normal muscular activity. So far I have not observed a single case that has come to operation where the rupture has been left alone since birth; and I have watched 119 herniae make a spontaneous disappearance without treatment.—I am, etc.,

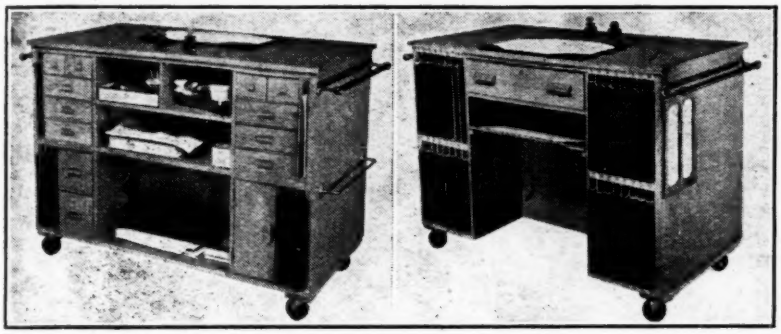
Bristol. GRACE E. WOODS.

Hillingdon Desk Trolley

SIR,—Prior to the war it was common practice to have case papers and records kept by the bedside of each patient. Personal records were accessible to the patients and were commonly read by patients and unauthorized persons. In an attempt to overcome this and to improve the case-paper record system, complete revision of case papers was undertaken at Hillingdon Hospital in 1937. So many inquiries

and requests have been made by medical staff who have used or have seen this system in use here that it is considered that a brief description might be useful.

The case paper is so designed that on the discharge of a patient the complete record can be read like a book, all the records being arranged in sequence and every relevant record included in the case paper. Different-coloured paper is used for radiological and pathological reports, special charts, etc., and these have a gummed edge for their attachment in sequence to the appropriately marked tab, which is a feature of this case paper. Case papers are coloured green, light blue, and mauve to denote male, female, and maternity cases, and are kept in special spring-back folders, numbered to correspond with the number of the bed occupied by the patient in the ward, and in order to ensure ready accessibility of these records I also designed the desk trolley which is illustrated here.



The purpose of the trolley is that it should contain the complete record of every patient in the ward and also hold blank forms for every investigation or request needed by the doctor. It also contains all equipment such as stethoscope, sphygmomanometer, auriscope, patella hammer, etc., required by the doctor conducting his examinations, and any equipment required for examination in special departments can be added. A bed list is attached to the trolley, numbered to correspond with the case papers, so that single case papers can be extracted when required. The trolley is wheeled round the ward by a member of the nursing staff when the doctor is doing his round, so that any appropriate records or requests can be made at the time. At all times, other than during the ward round, the desk trolley is kept in the sister's room, and used by her or the doctor as a desk.—I am, etc.,

Hillingdon, Middlesex. W. ARKLAY STEEL.

Test for Occult Blood

SIR,—I have read the article "A Simplified Benzidine Test" by Dr. Aneurin Hughes (November 1, p. 970) with great interest, and would like to congratulate the author on his work. Dr. Hughes has obviously studied the "occult blood" problem with care, and has devoted much time and thought to the difficulties and possible fallacies involved. One is surprised, therefore, to notice, in his preliminary discussion of the tests now in general use, the following remark: "Unfortunately Gregersen's reagent consists of a powder containing 0.2 g. of barium peroxide and 0.025 g. of benzidine dissolved in 5 ml. of 50% glacial acetic acid; and the solution requires to be freshly made up each day at least—anything but simple for the clinician, especially outside hospital practice."

In fact there are few, if any, tests in clinical medicine which are simpler to apply, with the possible exception of boiling the urine for albumin—and even then phosphates may yield a precipitate misleading to the unwary. The requirements are a supply of the special powders (wrapped in grease-proof papers that will keep indefinitely), a bottle of glacial acetic acid and one of distilled water, and a graduated 5-ml. glass cylinder with a glass stopper. The reagent is prepared by pouring into the glass cylinder glacial acetic acid up to the 2.5-ml. mark, adding distilled water up to the 5-ml. mark, and then introducing into this solution of freshly prepared 50% glacial acetic acid one of the special powders. The stopper is replaced, the cylinder is shaken, and the reagent is ready for use. Five or six specimens can be tested with the 5 ml. of solution thus prepared.

I am not here concerned with the clinical value of the test, but only with its applicability. I believe it to be a quick and easy test to use, both in and out of hospital.—I am, etc.,

Newcastle-upon-Tyne. A. G. OGILVIE.

SIR,—Dr. Aneurin Hughes (November 1, p. 970) describes yet another test for the detection of occult blood in the faeces. Having used the Gregersen slide test[1] almost daily in general practice for the past 20 years, I strongly disagree with him when he says of the G.S.T. that it is "anything but simple for the clinician, especially outside hospital practice." As he himself states, 5 ml. of a 50% solution of acetic acid is added to a prepared powder in a test-tube and applied to a faecal smear on a slide. What could be more easy and more simple? Harrison[2] actually commends it as a useful bedside test. The 5 ml. of 50% acetic acid can be carried in a small rubber-corked tube (such as is used to carry N/10 HCl in haemoglobinometer sets) into which is tipped the powder put up in waxed paper, in which it keeps indefinitely.

In some cases of sudden collapse, or suddenly developing unexplained anaemia, a faecal smear can be immediately obtained from the finger-stall after exploration of the rectum, and melaena perhaps discovered before even the patient is aware of it. In the consulting-room the Gregersen slide test takes only a few moments, and is more quickly performed than the usual test for sugar in the urine. There is no soiling of test-tubes with a faecal suspension, and only one tube is required. The thin smear of faeces is easily removed from the slide with a piece of cotton-wool. For convenience and economy, the powder can be made up in bulk. It is cheap, and in a dark bottle it will keep without deterioration for at least six months. It does not take long to learn the approximate quantity required and to tip it into the test-tube, either directly from the bottle or with the tip of a spatula. Should several different specimens or several samples of the same specimen have to be examined at the same time, I have found that the white glazed porcelain spotting plates with six or twelve scooped-out little hollows, such as are used in clinical laboratories, are admirable for the purpose. They show up the colours beautifully, have no sharp edges, and so are most easily cleaned. There is no necessity for the use of several small test-tubes, such as would be required in Dr. Hughes's test, for "pounding" purposes. These spotting plates cost only a few shillings, and can be bought from the laboratory furnishers.

It may prove that the simplified modification of the benzidine test described by Dr. Hughes has advantages, but, as he says himself, it has not yet been widely tried. On the other hand, the Gregersen slide test has for many years been used all over the world, and has stood the test of time. Ogilvie[3] established its suitability and freedom from fallacies, as Dr. Hughes himself points out and confirms. More recently Lipetz[4] described its value in general practice, and Needham and Simpson[5] its usefulness in a hospital out-patient department.

Whatever tests may be used in the detection of faecal occult blood, it seems important that they should be widely employed both in hospital and even more especially in general practice, where *x*-ray facilities are not so accessible and where the screening of gastro-intestinal conditions must in the first place be carried out. Only about one-third of

gastric neoplasms are immediately referred to hospital by the general practitioner,[6] yet Edwards[7] and many others have pointed out that occult blood is usually present in gastric neoplasm. Meulengracht and Jensen,[8] using the Gregersen slide test, found occult blood to be present in 89% of a series of 105 cases of alimentary neoplasm. Except in some obvious cases of cancer of the oesophagus and rectum, the diagnosis in all these cases was confirmed by operation or post-mortem examination. Hurst[9] and other workers have shown that in simple peptic ulcer also occult blood is present in a high proportion of active cases.

By the more general use of the tests for occult blood, earlier detection of gastro-intestinal ulceration becomes possible and in many instances the prognosis in alimentary neoplasm greatly improved. We should be grateful to Dr. Hughes for once more bringing these tests to our notice. A heavy responsibility lies on the shoulders of those of our teachers who fail sufficiently to emphasize their importance.—I am, etc.,

Edinburgh. S. LIPETZ.

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2 *Chemical Methods in Clinical Medicine*, 1947, 3rd ed., London.
3 *British Medical Journal*, 1927, 1, 755.
4 *Practitioner*, 1951, 166, 591.
5 *Quart. J. Med.*, 1952, 21, 123.
6 *British Medical Journal*, 1950, 1, 996.
7 Ibid., 1, 973.
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Cardiac Arrest

SIR,—During the past two months, five communications have appeared on the subject of sudden cardiac arrest during operation. Four were in the *Journal*—namely, Dark *et al.* (September 6, p. 533), L. Alexander and C. Langton Hewer (September 6, p. 546), annotation (September 6, p. 555), and A. W. Fowler (September 27, p. 723)—and one was in *Thorax*, McMillan *et al.* (7, 205). These several authors lay stress on differing causes of the condition and advocate differing methods of treatment with variable success. However, none of the authors lay primary stress on the all-important principle of establishing an artificial circulation and an artificial respiration at the earliest possible moment. It is most important to regard this condition as the indissoluble entity of cardio-respiratory arrest. The above authors recommend various procedures which may be successful in a few cases, but are not applicable to every case.

I wish to stress the utter importance of establishing an artificial respiration and an artificial circulation at the earliest possible moment. It is generally agreed that the brain cells are irreparably damaged if deprived of oxygen for longer than three and a half to five minutes. It is of course perfectly possible to resuscitate a person whose heart has stopped for longer than this period, but though the body may live the mind may well be dead and the patient become a living vegetable. Furthermore, it is obvious that a good coronary circulation must be provided if a normal spontaneous heartbeat is to be re-established. Artificial respiration is established by the anaesthetist by passing an intratracheal tube, or, if this is not available, using a face mask, and administering 100% oxygen under positive pressure, using the rebreathing bag of the anaesthetic machine.

Artificial circulation must be established by the surgeon using cardiac massage. It is important to regard the heart as a Higginson's syringe, and therefore the term "cardiac massage" is a misnomer; it would be better to say cardiac pumping or cardiac squeezing. In order to perform adequate "cardiac massage" it is essential to open the chest. This may be done very quickly through an anterior intercostal incision in the third or fourth left interspace, using a scalpel only. The pericardium must be opened widely and the heart grasped firmly in the hand, and vigorous and purposeful squeezing begun at the rate of 40–60 to the minute. The anaesthetist should check that the cardiac massage is adequate by feeling a carotid pulse. By this means, contrary to what McMillan *et al.* say, it is perfectly possible to maintain a systemic blood pressure of 70–80 mm. Hg. An artificial carotid and coronary circulation is established, and adequately oxygenated blood reaches the brain cells and the heart muscle, and the patient is artificially alive. The immediate crisis is averted, and the next steps to establish spontaneous rhythmic heartbeat may be considered. Very frequently a few minutes of adequate "massage" is all that is required, but, failing this, 3–4 ml. of 10% calcium chloride injected into the cavity of the left ventricle, as advocated by Blalock and Kay, may prove remarkably effective. If the ventricles are fibrillating, defibrillation will be required, and is best performed by electric shock as advocated by McMillan *et al.* But these latter procedures are all secondary to establishing an adequate carotid and coronary circulation with adequately oxygenated blood within three and a half minutes of the cessation of the heartbeat.—I am, etc.,

Bristol. ERIC M. NANSON.

SIR,—Dr. F. Coyne asks (November 8, p. 1046) what constitutes the longest period of cardiac arrest with complete recovery. Touroff and Adelman (*J. Amer. med. Ass.*, 1949, **139**, 844) report a case with cardiac arrest for 40 minutes followed by rapid and complete recovery.

It would appear in Dr. Coyne's case that circulatory, as opposed to cardiac, arrest existed for approximately six minutes. The successful outcome, for which all present share the credit, is evidence that an efficient circulation was maintained for the remainder of the 24 minutes. What matters is the delay in restoring circulation by massage and not the duration of cardiac arrest.—I am, etc.,

Manchester. TOM DINSDALE.

Treatment of Congenital Deformities

SIR,—In "Any Questions?" (October 4, p. 790) a query about valgus ankles in young children receives the answer that "between 1 and 2 years no treatment is advised." In your issue of November 1 (p. 980) there is a review of a book on congenital dysplasia (and dislocation of the hip) by Vernon Hart, in which it is stated that the earlier treatment of this condition is begun the better are the results. I suggest that this indisputably correct teaching on congenital dislocation of the hip applies also to the related condition of congenital valgus talipes or flat feet, and that they, and any other moulding deformities of babies' feet, should be diagnosed at birth and put right before the child needs the foot to stand on. Of the three stock congenital mouldings of the feet, metatarsal varus and valgus can be permanently corrected before 10 months of age; while the misnamed "equino-varus," or club foot, should after that time need only maintenance of the correction gained. None of these deformities, however, will be understood until orthopaedic surgeons in general give up that curious "intrauterine Monroe doctrine" which will not allow that any mechanical forces can deform the foetus. Anyone who studies the theory of intrauterine forces will see:

(1) That dysplasia and dislocation of the hip are separate conditions, so that congenital weakness of the hip can occur without dislocation in the absence of sufficient intrauterine thrust on the knee to push out the head of the femur. Thus many authors would be saved the absurdity of describing all the signs of dislocation in a hip which they insist is not dislocated, as well as such verbal quibbles as saying there is an "ectopia" of the head of the femur although not a dislocation; while the student would not need to try to see a clear meaning in the term "pre-subluxation."

(2) Why metatarsal valgus is very common with congenital dislocation of the hip, since the same increase of intrauterine pressure that bends the foot round the outer side of the leg also forces the head of the femur out of the weak socket of dysplasia by a thrust on the knee.

(3) Why varus deformities of the foot are extremely rare with congenital dislocation of the hip, since the pressure on the outer side of the foot that causes them keeps the knees in abduction, and consequently the heads of the femora in their sockets.

(4) Why much the easiest way of reduction of a dislocation is to reverse the thrust on the femur, while it is in the intrauterine position in which the displacement occurred.

(5) Why valgus deformities of the foot are invariably accompanied by weak muscles, the increased pressure that produces the one effect also producing the other.

(6) Why in the extreme degrees of congenital dislocation of the hip the muscles are ruined and the joints stiffened by the extreme pressure that has produced these effects (the "teratological type" of Hass, the "foetal type" of Hart, or my "compression baby").

(7) Why, when the bones are unduly weak as in osteogenesis imperfecta, the femora frequently show congenital bowing along their shafts or in their neck from the intrauterine thrust.

(8) Why the most efficient method of correcting moulding deformities of the feet is to reproduce the kind of force that caused them—that is, to use a soft, widely distributed, continuous but pulsating pressure. The pulsations, which enable heavy pressure to be used without trouble from shutting off the blood supply, can be supplied by that continuous kicking of the infant which the classical plaster-of-Paris so effectually prevents.

A similar principle is that to control the limbs, which move by a series of levers, a countervailing series of levers is far more efficient than the classical "cases" of plaster or metal. It is only necessary to study the published modifications of my hobble splint to see that most orthopaedists do not realize that it is a series of levers at all.—I am, etc.,

London, W.1. DENIS BROWNE.

The Patient's Verdict

SIR,—May I congratulate Dr. R. W. Cockshut on his letter (November 1, p. 993) commenting on Lord Moran's oration? He has hit several nails right on the head.

Like all converts, Lord Moran seems to see no good in our profession's past history and no possible evil in State-controlled medicine, new in England but not abroad. He still seems to believe in the idea of automatic "progress" based on science, though he seems to admit that the wholly "scientific" approach to medicine has tended to lose sight of the fact that all medical practice is an art which teaches us to treat not merely physical symptoms but the patient as a living sentient being strangely compounded of body and soul. To become competent in this art a student must surely know something of our profession's history and much about human nature.

The medical profession was once classed as a learned profession. Its members were taught at our ancient universities, themselves church institutions, and the basis of all instruction was theology and philosophy. The late Professor Ralph Stockman, of Glasgow, used to tell his students that we should make better doctors if we knew our Bibles and Shakespeare than if we knew the *B.P.* by heart. It has been said, and I think truly, that forms of government and institutions are the direct outcome of the religion or philosophy which is commonly accepted by any society. Hence, I think Lord Moran is wrong in advocating an extension of State control of medicine to those who, as our successors, will mould the next phase of medical practice unless he is also prepared to advocate acceptance of the philosophy upon which State control of the individual in general is based.

The picture as I see it is one of an older system with its voluntary hospitals in particular, which was derived from the teaching of the pre-Reformation Church (the *Ecclesia quod est in Anglia* of Magna Carta), and its replacement by a system based on the philosophy of Marx and Nietzsche. "Like produces like." "Thoughts become or beget things and institutions." We have seen in Germany what degraded forms of medical practice resulted in Belsen from State medicine. It has happened in Russia. It may take longer here, where the Christian tradition and its derived standard of ethical values are still potent, but those who teach our present-day students should themselves be clear as to which philosophy they accept before denouncing our past.

That reforms were overdue is admitted, but the politicians are not the people who should have tampered with the system, especially the hospitals. It is useless to spend time in arguing over details of administration of a system if its basic philosophy has been seen in practice to degrade the medical profession. For reference see William Cobbett's *History of the Protestant Reformation* (with reference to the origin of voluntary hospitals), *The Road to Serfdom*, by Hayeck, and *Heil Hunger*, by Dr. Martin Gumpert. There are many others, including Hitler's *Mein Kampf*.—I am, etc.,

Bournemouth. DAVID HARDIE.

Oxygen Administration in Asphyxia Neonatorum

SIR,—I should like to draw attention to one or two points arising from the article by Drs. Donough O'Brien and Hilda Roberts on oxygen insufflation in the treatment of asphyxia neonatorum (November 1, p. 963). There is no doubt that this is a most useful method of resuscitation and not used often enough, but I would seriously question whether endotracheal intubation was always necessary.

The authors themselves admit that "inserting the tube and changing it when blocked . . ." is badly tolerated by premature infants, but surely the same is true for many full-term babies who are suffering from severe asphyxia. In my small experience, the more carefully such babies are handled and the less mechanical interference with them the better. Cardiac inhibition due to vagal administration is always possible, and the introduction of a potentially infected foreign body into the trachea so early in life could lead to respiratory infection.

I have found the following routine to be quite effective. Allow the attendant midwife about three minutes to wrap up the infant and to suck mucus and fluid from the mouth and pharynx. Oxygen is then led to the baby through an ordinary female rubber catheter at about 2–3 litres per minute (that is, a stream of oxygen that can just be heard). The end of the catheter is placed in the child's mouth, the lips are pursed around the catheter by the thumb and fingers of the doctor's right hand, while the infant's nostrils are simultaneously closed by the thumb and forefinger of his left hand. At once the chest will be seen to expand, and both hands then relax to allow the chest to deflate. The inflation and deflation of the lungs can be rhythmically continued by the doctor for as long as necessary, but in a successful case spontaneous respiration often starts very soon. There is absolutely no disturbance of the infant, and, unless brute force is used, it is impossible to blow the lungs up excessively—as I once saw happen when a well-fitting endotracheal tube was in position. It is almost impossible to get a completely air-tight fit between the lips and the catheter, and therein lies the safety of the method.—I am, etc.,

London, N.18. G. S. A. KNOWLES.

Infectious Mononucleosis with Thrombocytopenic Purpura

SIR,—The article on "Infectious Mononucleosis with Thrombocytopenic Purpura" by Drs. C. M. Ogilvie and T. E. Parry (November 1, p. 977) prompts me to send details of a similar case.

A 14-year-old schoolgirl was admitted to the Canadian Red Cross Memorial Hospital in February, 1950, because of jaundice of some 10 days' duration which had been preceded by sickness and general malaise, but not by any throat infection. She had noted that her stools had been clay-coloured and her urine dark. Three days after the onset of jaundice she noticed the appearance of petechiae on her chest and neck; these were at first few in number—later becoming numerous and coalescing in places to form bruises. These skin appearances were followed by frequent and severe epistaxes and haematuria. As these bleeding symptoms appeared, the jaundice had faded. There was no melaena. Joint pains were severe immediately before admission, but at no time was there any evidence of haemarthrosis. There had been no previous episodes of bleeding and no significant past or family history was obtained. On examination she was pyrexial, slightly jaundiced, and there was a widespread purpuric rash on the chest, abdomen, limbs, and mucosae. Her throat was healthy. There were small glands in both axillae, but no other adenopathy. The liver edge was palpable, and the spleen could also just be felt, appeared firm, and was not tender.

The haematological picture revealed a moderate degree of anaemia and a mononuclear leucocytosis; the platelet count was 30,000 per c.mm. and examination of her bone marrow showed the presence of many typical glandular fever cells. The diagnosis of infectious mononucleosis was finally confirmed by a strongly positive Paul-Bunnell reaction (1:896). Hess's test of capillary fragility was strongly positive. Agglutinations against the leptospiras were all negative. In spite of repeated transfusions with fresh blood the patient continued to bleed profusely from her nose and gums and fresh purpuric spots appeared. The platelet count had decreased to 4,000 per c.mm. on March 2, but as the haemoglobin level was 106% at this time it was decided not to carry out any further transfusions unless the patient became anaemic. Her condition improved gradually and the bleeding diminished in amount, then ceased completely.

On March 14 she was well and symptom-free and was getting up. On examination the spleen was no longer palpable. There were still some fresh petechiae on the chest. Haemoglobin was 79%, white blood count had reverted to normal, and the platelet count was 48,000 per c.mm. Hess's test was still positive. She was discharged one month later despite the fact that the platelet count was only 20,000. She remained perfectly well and was seen at regular intervals in the out-patient department. The platelet count steadily returned to normal.

Though both jaundice and thrombocytopenic purpura are described as complications of infectious mononucleosis, it is extremely uncommon for them to appear together in the same patient. In our case the bleeding symptoms were so severe as to cause anxiety and require transfusion. The patient, however, made a complete recovery and the haematological picture reverted to normal.

I wish to thank Dr. G. D. Hadley, under whose care the girl was admitted, for permission to publish this case.—I am, etc.,

London, S.W.10. S. BENAIM.

Asthma in Childhood

SIR,—I am pleased to note that Dr. C. B. S. Fuller in his article (September 20, p. 636) has made a special heading of the treatment of associated nasal diseases. So frequently one sees cases of asthma in children and adults treated for long periods by paediatricians and allergists without any improvement in spite of intensive therapy, while an ear, nose, and throat examination may have revealed nasal blockage with purulent sinuses or deflected septum, etc. From his figures I notice that almost two-thirds of his total of 209 children surveyed had some form of ear, nose, and throat (including tonsillectomy and adenoidectomy) operation performed.

This close association of asthma and the nose and throat is not widely and sufficiently appreciated. Rather the tendency has been to point a guilty finger at the otologist for tonsillectomy as a precipitating factor in the causation of asthma.—I am, etc.,

Johannesburg. J. FINE.

Intestinal Worms

SIR,—In connexion with the refresher course on intestinal worms (November 1, p. 988) I would like to comment that when *Enterobius* infestation is determined in a child it is often well to consider treatment of the whole family, even though they do not present symptoms. I have found that gentian violet, enteric coated, given in 30-mg. doses three times a day to children for 10 days, and double this dose for adults for 14 days, is often effective provided, as pointed out by the author, reinfection is prevented.

Relative to *Trichinella spiralis* in swine, it can be pointed out that, as long as pork scraps go into garbage and garbage is fed unboiled, the cycle will continue. Pork in small pieces kept in a deep freeze for 20 days at 5° F. (−15° C.) or for 24 hours at −0.4° F. (−18° C.) is safe to use even though heavily contaminated with cysts of the *Trichuroidea*.—I am, etc.,

United States Air Force, Arrington, Cambs. CHARLES H. MORHOUSE.

Recent Advances in Active Immunization

SIR,—Dr. H. J. Parish (November 8, p. 1010) gives one of his masterly summaries of recent advances in immunology.

At times, however, he appears to have mislaid a page of his manuscript, or to be looking through the wrong end of his telescope. For instance, the bibliography at the end makes no reference at all to a certain Dr. L. B. Holt, who during the last few years has been largely responsible for shaking the science of the development of diphtheria prophylactics from the slough of complacency into which it had fallen. As is universally known, Holt is the father of P.T.A.P., which is now rapidly ousting all other forms of diphtheria prophylactic in Europe. In the five and a half lines devoted by Dr. Parish to this important development I do not find the name of Holt at all. How nice to be so important that one's name requires no mention. In the 36 lines allotted to our old friend A.P.T. and allied matter the telescope has certainly been turned round the right way. A few people may think that there are other trifling omissions from this carefully considered bibliography.—I am, etc.,

London, S.E.5. GUY BOUSFIELD.

"Refresher Course" Book

SIR,—May I be allowed to congratulate you on the excellent volume of combined "Refresher Courses" published weekly in the *Journal*?

I sincerely hope that in the future there will be a regular annual edition.—I am, etc.,

London, W.1. E. P. SCOTT,
President of the Section of General Practice, Royal Society of Medicine.

POINTS FROM LETTERS

Foreign Body in Arm

Dr. EDWIN J. RIX (Birmingham, 18) writes: I was interested to read Dr. L. Sheldon's account (November 8, p. 1047) of a sewing-needle in an arm, as I recently had a similar case. A lady consulted me about five weeks ago complaining of pain in the left elbow region. Examination revealed a foreign body (which I thought to be a needle) lying subcutaneously on the posterolateral aspect of the elbow. I inquired whether the patient had ever received injections into that arm, and was rewarded with a history of a hypodermic needle being broken in the arm about a year ago. However, when I removed the needle I found it to be of the sewing variety, some 3 cm. in length, rather rusty, and without its point. There was a well-marked fibrous reaction around it. The patient could suggest no explanation of the presence of this needle and had no recollection of an injury with a sewing needle.

The Offending Foreskin

Mr. H. L. PEAKE (Eldoret, Kenya) writes: It is generally agreed that carcinoma of the penis is confined almost entirely to the uncircumcised. To quote only one authority, *The Medical Annual*, 1950, states, "All observers agree that circumcision in the first five years of life protects absolutely from penile cancer; this applies not only to one group, such as the Jewish, but equally to the mixed races of the U.S.A." You quote an estimated death rate of 16 per annum due to circumcision. It should be quite simple to ascertain the annual death rate from carcinoma of the penis. Finally, it might easily be possible to reduce the circumcision death rate if the causes were more widely known, since it is often done in a hurried and rather haphazard manner.

Air Pollution and Lung Cancer

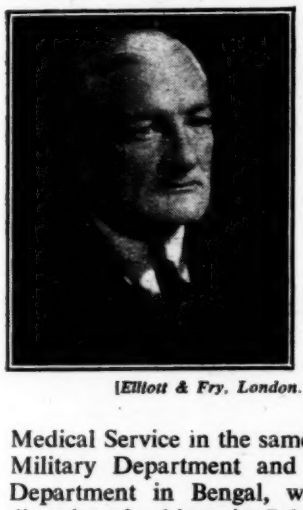
Dr. HANDLEY B. HOWELL (Bristol) writes: It is an accepted fact that there are three dangerous groups of carcinogenic agents to be found in atmospheric dust as stated in your article (November 1, p. 982). The important point to establish is their source. It is noted that this is attributed chiefly to the smoke of domestic and factory chimneys. Last year I carried on a considerable correspondence in the *Lancet*, but we did not reach much conclusion in the matter. I am, however, still convinced that the most dangerous sources of these carcinogens are the exhaust fumes of all engines fuelled by diesel oil, and the smoke and fumes from furnaces using these oils in steam-generating and water-heating plant of all kinds.

Obituary

Sir DAVID MUNRO, K.C.B., C.I.E., LL.D., M.B., F.R.C.S.Ed.

Air Vice-Marshal Sir David Munro died at Halton, Buckinghamshire, on November 8, in his 75th year. He had led a full life, crowded with varied activity in work and play: his enjoyment of it emerges vividly from his autobiography, *It Passed Too Quickly*, published in 1941. He had a wide popularity, effortlessly won by his sincerity, his gift for fellowship, his sense of humour, his prowess at games, and his zest in all things. He held a sequence of important positions, and always with success.

David Munro was born at Elstree, Hertfordshire, on June 23, 1878, the twelfth child of a schoolmaster. He went up to St. Andrews University, in an Eton suit, at the age of 14 and remained there for six years. There as a fellow-student he met his future wife, Isabel, daughter of Dr. J. Cunningham, of Campbeltown, Argyll. They were married in 1905: he is survived by her, and by their son, daughter, and grandchildren.



[*Elliott & Fry, London.*

In 1898 Munro went to Edinburgh University, graduating M.B., Ch.B. in 1901. He joined the Indian Medical Service in the same year, and was at first in the Military Department and later in the Civil Military Department in Bengal, when he also lectured on a diversity of subjects in Calcutta University. He became F.R.C.S.Ed. in 1911. In the 1914–18 war he served in a hospital ship and in France, Palestine, and Mesopotamia. He was created C.I.E. in 1917. He transferred to the R.A.F. in 1919, becoming Principal Medical Officer at its headquarters in India. In 1921 he was appointed Director of R.A.F. Medical Services. He held this post at the Air Ministry until 1930, an unusually long period, and had great influence upon the development of the new service in its formative phase. He has summed up his policy: "If I had one ideal for my new medical service it was that the officers should be doctors first and not become too military, and I believe it was attained; conversely, that they should be an integral part of the R.A.F. organization and not a Service within a Service." He was created C.B. in 1924 and K.C.B. in 1930, and was an Honorary Surgeon to the King from 1925 to 1930.

Munro retired from the R.A.F. in 1930 and was appointed by the Medical Research Council to their headquarters staff as secretary of the Industrial Health Research Board. Here he encountered a new aspect of the scientific problems of men and machines with which he had become familiar at the Air Ministry. He made a valuable administrative contribution by a policy of integrating the investigating staff more closely with that engaged in other lines of medical research and of basing the field workers on university laboratories. He held the position, latterly on a part-time basis, until 1942. The war of 1939–45, however, brought an additional call for his services. In 1940 he was appointed Chief Medical Officer of the Ministry of Supply, to deal with medical questions arising at Royal Ordnance factories. He retired in 1943 but remained a medical adviser to the Ministry. He had also been vice-chairman of the board of management of the London School of Hygiene and Tropical Medicine, and was a member of the Factory Welfare Board of the Ministry of Labour and of the School Council of St. Thomas's Hospital. He was Master of the Skinners Company in 1942–3.

It is impossible to think of David Munro without recalling his skill as a golfer and his love of sport and particularly of horses. In India there were polo, pig-sticking, and shooting many kinds of game. In England he played polo, rode to hounds, and at the age of 58 took part in his first steeplechase. In his seventies he took up gliding with the enthusiasm of a youth.

Of all his many honours none pleased him more than to be elected by the students to be Rector of St. Andrews University in 1938. The honorary degree of LL.D. of the university was conferred on him in 1939, when he was installed as Rector. Owing to the war he held the office until 1946; and, whereas for some men it would have been a sinecure, for him it was another outlet for his energy and keenness. He wrote: "I felt myself at the zenith of my career. I had left home to begin life in St. Andrews. To St. Andrews at the last I had returned."—A. C. T.

We are indebted to Air Marshal Sir VICTOR RICHARDSON for the following appreciation:

Sir David Munro came to the Royal Air Force as Director of Medical Services in 1921, after being in the Indian Medical Service, and continued in office until 1930; he was successor to General Sir Matthew Fell—the first D.M.S., and indeed the father of the R.A.F. medical branch. In the I.M.S. Munro's work had lain largely on the civil and specialist side, and he was therefore, as occasion demanded, able to take a detached and unbiased view of the general and peculiar medical needs of the Air Force. Among the problems of those days were the stabilization of the list of medical officers and the inclusion in it of a specialist group to cover the particular needs of the Service, the establishment of Air Force hospitals, and the development of a nursing service. The determination of the permanent list of medical officers by seniority proved to be a thorny matter, as doctors working with, or later commissioned in, the Air Force came not only from the fighting Services but also from civil life, so that varying factors came up for consideration and many difficulties had to be met and solved. The integration of the specialist group to deal with the peculiar needs of flying personnel (ophthalmology, otology, psychology, physiology, and tropical medicine, as well as straight medicine and surgery) called for careful planning and discriminating selection, though much help was forthcoming from the Air Ministry Medical Advisory Board of eminent doctors and scientists in civil life. Apart from the question of their special requirements, Air Force personnel are happier in their own hospitals, cared for by their own medical and nursing staffs, and the need for hospitals was dealt with by the building at home of the first new R.A.F. hospital at Halton, Bucks, and the further development of the R.A.F. Officers' Hospital at Uxbridge, Middlesex, while overseas hospitals were established at Bagdad in Iraq, in Aden, and in Palestine. Not less pressing was the call for a first-class nursing service, which emerged as Princess Mary's Royal Air Force Nursing Service. These, then, were some of the problems that had to be dealt with during the evolution of the Medical Service: that they were successfully handled in a large measure between 1921 and 1930 is no mean tribute to the memory of the then D.M.S.

Air Vice-Marshal T. C. MORTON writes: Sir David Munro was the third Director-General of the R.A.F. Medical Branch, but to all of us who served with him from its foundation he was recognized as its father. Surgeon Captain Munday, our first Director, was a naval surgeon; General Matthew Fell, the second Director, came to us from the R.A.M.C. He laid the foundations, truly, but left us very shortly to become Director-General of the Army Medical Services. It was, however, due to Fell that Munro, a young I.M.S. major who had served under him in Mesopotamia, was seconded to the R.A.F. to proceed to India as the first R.A.F. Principal Medical Officer, with the rank of wing commander. It was a fortunate choice, for only a man with 20 years' experience in India could have dealt with the teething troubles of a new Service in such a well-entrenched Army preserve. He left India a bare 18 months later to succeed Fell as Director-General, and promptly entered the arena to serve as a member of the Cabinet committee to decide whether there should be a separate R.A.F. medical branch or whether it should be taken over by either the Army or Navy medical services. Subordination no, co-ordination certainly: the battle was won, for David Munro was a "bonny fechter" with a silver tongue. During his nine years as Director-General he was strongly supported by Lord Trenchard, and so the R.A.F. Medical Branch came into being and the camaraderie between the flying and medical branch was cemented for all time.

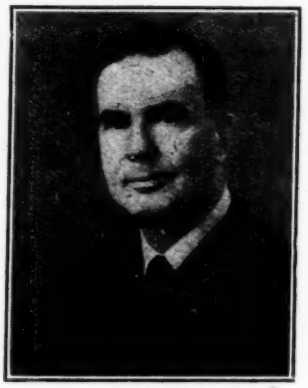
Sir David Munro, the man himself, was one who warmed both hands before the fire of life. Fear was a stranger to him, and, blessed with excellent hands and a good eye, all games came easily to him. A scratch golfer, he represented the R.A.F. on many occasions. A keen rider to hounds with the Old Berkeley and Whaddon Chase, an enthusiastic polo player, Sir David believed that the best view of the world was between the ears of a horse. At 58 he rode his first of many point-to-points, but, if the truth be told, with many falls, for he was a thruster. He preached the dogma, and who will gainsay him, that "guts count as high as brains," and he was the fortunate possessor of both in ample measure. Socially he was a *bon viveur* and an ardent clubman, with a discriminating palate, a pretty wit, and, if warranted, a blistering tongue. At 75, as commanding officer of the local A.T.C., he plunged with enthusiasm into the art of gliding, piloting his glider over the countryside in his beloved Bucks, and gazing nostalgically from 300 feet over the scene of his past athletic triumphs. He always felt that the zenith of his career was reached when he was installed Lord Rector of his own University of St. Andrews in 1939, and it was then that he quoted these lines, written by himself when he summed up his creed:

> But when our interests cease, emotions fail,
> When we can love no more, nor fight, nor sin,
> No longer strike a ball nor tell a tale,
> Then let us pass—what is there left to win?

J. ERIC STACEY, M.D., F.R.C.S.Ed., F.R.C.O.G.

By the death of Mr. J. E. Stacey on November 9 the science and art of obstetrics and gynaecology has lost a skilled exponent, the Royal College of Obstetricians and Gynaecologists a wise counsellor, and the medical faculty of the University of Sheffield an experienced and popular teacher.

John Eric Stacey was born on February 17, 1893, and was educated at Christ's Hospital. He won the open medical scholarship at the University of Sheffield, where he graduated M.B., Ch.B., with honours, in 1913, being awarded the gold medal in clinical medicine and surgery. He became a resident house-surgeon at the Jessop Hospital for Women at Sheffield, but when war broke out in 1914 he volunteered immediately and was posted as a combatant to the Royal Berkshire Regiment. He later transferred to the R.A.M.C. and served as regimental medical officer to the same unit. He suffered a serious spinal injury at the battle of Loos which caused a complete paraplegia, as the result of which he was bedridden for eight months. Those who witnessed his determination to recover, when once it was clear that there was hope, will never forget the supreme demonstration he gave of the influence of mind over matter. In 1918 he did most useful work as a surgeon at the Third Northern Hospital at Sheffield, standing for long periods in operating theatres with the aid of surgical appliances, and he was a source of inspiration and encouragement to many wounded soldiers. He celebrated his recovery when the war was over by undertaking a bicycle tour in Italy and the Dolomites with a medical friend.



Stacey had determined to make obstetrics and gynaecology his career and he was appointed registrar at the Jessop Hospital for Women. In 1920 he became a Fellow of the Royal College of Surgeons of Edinburgh. At that time the only higher degree in his specialty was the M.D. of London. To obtain this he took the M.B., B.S. of the University of London by examination in 1921, proceeding M.D. in obstetrics and gynaecology in the following year. He was appointed honorary assistant surgeon at the Jessop Hospital in 1924 and full surgeon in 1935, and became senior surgeon last year. He was also honorary consultant surgeon to the Beckett Hospital, Barnsley, and to the Retford Cottage Hospital, and was lecturer in obstetrics and gynaecology in the University of Sheffield for many years. Stacey was elected a Fellow of the Royal College of Obstetricians and Gynaecologists in 1937. He was a founder member of the College and was a member of its council from 1930 to 1937 and again from 1941 to 1947. He had been a vice-president of the College since 1949. He was a member of the travelling club of obstetricians and gynaecologists, and last year he visited Canada and the U.S.A. as a representative of the College. During the last week of his life he was elected an Honorary Fellow of the Royal Society of Obstetricians and Gynaecologists of Athens, but unfortunately he was too ill to appreciate it.

Stacey had a wide experience as an examiner in his specialty for the universities of Sheffield and London and for the diplomas of the Royal College of Surgeons of England, the Royal College of Obstetricians and Gynaecologists, and the Central Midwives Board. He made outstanding contributions to the literature of his specialty, and his paper on "Failed Forceps," which was published in the *British Medical Journal* in 1931, has an international reputation. He also contributed the article on the external female genital organs to Volume 4 of *British Surgical Practice*. Other articles from his pen appeared in this *Journal* and in the *Practitioner*. He read a paper on "The Logical Approach to Prolapse" before the International and Fourth American Congress of Obstetricians and Gynaecologists in 1951. When the British Medical Association held its Annual Meeting at Winnipeg in 1930 he acted as honorary secretary of the Section of Obstetrics and Gynaecology.

Eric Stacey had a vivid personality and a great courage, both moral and physical. His greatest attribute was a fearless sincerity and a determination not only to do what he himself thought was right but also to convince others to have the same opinion. He was tolerant, however, and would listen to opinions contrary to his own, and was never ashamed to confess when he had judged unwisely. In other words, he was a good loser and he bore no ill will or vindictiveness towards his opponents.

After the National Health Service Act was on the statute book, he did his utmost to make it work in the interest of the patient. That was his paramount purpose, and it took precedence over all other aspects in any discussion. His manner and his choice of words were sometimes too direct, even aggressive, so that some might take offence, but his active and always logical opposition was really a great stimulant. To the student he was always a teacher who, though dogmatic, had a sound reason for his opinion, and he would spare no pains to explain any problem. His witticisms were of great value to the successive editors of the students' magazine, but they left no sting. His students will in after years appreciate the principles of their craft which he taught them. He had no use for sham, and he impressed on them that experience and example, combined with single-mindedness and integrity, were the most necessary qualities of a good teacher. He appealed to them all by his perennial youth.

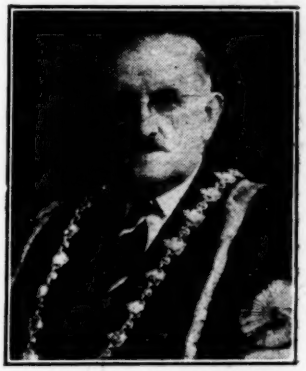
Eric Stacey owed much to his devoted mother, who was widowed at an early age, and much to his wife, formerly Margaret Reid, who is a medical graduate of the University of Aberdeen. She was a great companion and helpmate to him throughout their life together and gave him her devoted attention during his last illness. Only those who have received hospitality in their beautiful Derbyshire home can realize what a great loss his death is to her and to his many friends. Our sympathy goes out to her and to her son and daughter at this time.—E. F. and J. H. C.

H. S. MEADE, M.Ch., F.R.C.S.I.

Mr. H. S. Meade, who died on November 11 at St. Vincent's Hospital, Dublin, after a trying illness bravely borne, was in his 68th year. He had become one of the most widely known of Irish surgeons, and for many years past had been so familiar a figure at many European surgical congresses that an English colleague had affectionately dubbed him "Ireland's ambassador of surgery."

Born in Amoy, S. China, on December 3, 1884, where his father had been a member of Sir Robert Hart's staff, Henry Sords Meade lost his parents in an epidemic of cholera at a very early age. He came home to relatives in Dublin, by whom he was educated at the Carmelite College. From there he entered the Catholic University Medical School of Newman's foundation in Cecilia Street, where his student course was marked by an unbroken succession of honours and medal awards. He qualified L.R.C.P.&S.I. in September, 1909. Almost immediately he was appointed house-surgeon at St. Vincent's Hospital, where he came under the intimate direction of the late "Johnnie" McArdle, the dynamic professor of surgery in University College, Dublin, whom he was to serve more closely for many years as first assistant. As a student he had shown a particular penchant for anatomy, and, his term of hospital residency completed, his first teaching appointment was that of demonstrator of anatomy in Professor E. P. McLoughlin's department in the medical school. In 1910 he took his F.R.C.S.I., and in the year following was appointed assistant surgeon to St. Vincent's Hospital.

On the outbreak of war in 1914 Meade joined the French Army, being posted to Villeneuve-sur-Lot as *Médecin-major*. For his services he was awarded the Médaille de la Reconnaissance Française, and later was appointed Chevalier de la Légion d'Honneur. Returning from France, he joined the R.A.M.C. with the rank of captain, serving as surgeon in the hospital ship *Mauretania* in the Mediterranean.



[Irish News Agency.

Resuming his post at St. Vincent's, he showed himself resolute and tireless in the pursuit of his studies and perfection of technique. Unsparing of his time and energy, he was often unconventional in his methods. His patients knew his kindness and his understanding, as they appreciated his skill, and scores of them became his personal friends. One sometimes heard talk in those early days of "Meade's luck": he had his strokes of deserved good fortune, but the real secret of his success throughout his life lay in his foresight and his careful preparation. "No man," said Sir Humphry Rolleston, "can tell what is in store for him, nor command success, but he can do better by deserving it."

In 1928 Meade succeeded his old chief as professor of surgery at University College, Dublin. Never a facile speaker, as a teacher he was dogmatic, factual, accurate rather than brilliant; at the bedside he preferred to teach by the Socratic method of question and answer rather than by the set exposition of a particular subject. One can still hear his frequent, "Did you look?"—his favourite theme being that for one mistake due to ignorance nine were due to lack of observation. As an examiner he was patience personified, and utterly fair: no student ever found him testy or irritable or left the ward or the examiner's table feeling that he had not had a fair deal. In the theatre Meade was almost tireless, and there, as a teacher, he was perhaps at his best. A skilled anatomist, with the lightest of hands, he never seemed to hurry, even in moments of real emergency: calm and imperturbable, he was ready for all occasions. He had a love of mechanical things and delighted on his return from visits abroad to demonstrate the latest thing he had purchased in instruments. In this present era of specialists he remained the finest exemplar of the first-class general surgeon, equally at home in many fields. As a colleague he was outstanding for his integrity, his steadfast honesty, his frankness—not flashy qualities, these, but invaluable in a friend to whom one might turn in any difficulty for assistance, and never in vain.

He travelled widely, and knew most of the leading British and European surgeons well. Many honours came to him, yet no man had a more innate modesty. President of the Irish College of Surgeons in 1948–50, he was elected President of the Association of Surgeons of Great Britain and Ireland in 1950. He was a member of the British Orthopaedic Association and an associate member of the French Academy of Surgery; he had

been a member of Council of the International Society of Surgery, and only a few weeks before his death had been elected an honorary member of the Belgian Society of Surgery.

No man was more hospitable. His home was one of the prominent social centres of Dublin, and in it he and Mrs. Meade delighted to entertain a host of friends. He had worked hard and played little through an active life, yet he seemed to be almost ageless. His unexpected return in the first days of a summer vacation after the B.M.A. Annual Meeting in Dublin last July, when he served as a vice-president of the Section of Surgery, came as a shock to his friends and colleagues alike. His days were numbered, but he faced the end as imperturbably as he had faced life itself; no one heard a word of complaint or self-pity fall from his lips. With Abraham Lincoln, he "did the best he knew how, the best he could, and he kept on doing it to the very end." He had a full and a happy life, but for his immediate colleagues his going leaves "a lonely place against the sky." To his widow—who was the perfect partner and helpmate—to his daughter and his sons will go the sympathy of hundreds of his patients, friends, and colleagues in their tragic loss of a gay and gallant companion.—W. D.

Professor LAMBERT ROGERS writes: Few surgeons can have travelled as widely in Europe or known the Continent and Continental surgeons as well as did Professor Harry Meade, and to have been abroad with him and seen him as at home in a foreign city as in his own Dublin was an experience to be remembered. For many years he was the Irish delegate to the International Society of Surgery, at the meetings of which body he did a great deal to enhance and maintain the prestige of Dublin surgery. He was a fine linguist, a great surgical craftsman, a widely read general surgeon with a leaning towards orthopaedics, and an occasional writer who contributed a number of papers to the *Irish Journal of Medical Science*, edited by his friend and colleague, William Doolin. Honours rightly came to him: in 1934 the M.Ch., honoris causa, of the National University, in which he occupied one of the chairs of surgery; in 1948 the presidency of the Royal College of Surgeons in Ireland; in 1950 the presidency of the Association of Surgeons of Great Britain and Ireland; and from time to time honorary membership of various foreign surgical societies. But all such honours sat lightly upon him and had no visible effect on his tall, spare, distinguished appearance and his kindly personality. Above all else Harry Meade was a charming and courteous host, a delightful companion, and a happy family man, and to stay in his house was to enjoy very real hospitality. To meet him at any time, anywhere (perhaps in Paris, Madrid, or Berne), was always a joy and to know him a privilege. To examine candidates with him and his friendly colleague, Professor H. L. Barniville, was to know how pleasant an occasion could be made of what might otherwise have been an exacting and dull affair. Many surgeons in many countries will miss him and sympathize with Mrs. Meade and his family and with his colleagues in that fair city of Dublin in which for many years he has been a beloved and much respected leader in his subject.

J. C. MARTIN, L.R.C.P.I.

Dr. James Charles Martin, who died on October 18 at his home at Ballsbridge, Dublin, was the son of an Inspector-General of the Bank of Ireland, and received his early education in England, returning to Dublin for his medical studies. He qualified L.R.C.P.&S.I. in 1894, and, after holding appointments at the Lying-in Hospital and the Mater Misericordiae Hospital in Dublin and as a ship surgeon, he became assistant medical officer, and later resident medical superintendent, at the Letterkenny Mental Hospital in County Donegal. He resigned his appointment at the hospital in 1936, having completed the statutory period of service. He then became the first medical secretary of the Irish Free State Medical Union (Irish Medical Association and British Medical Association), which was formed with the object of uniting the branches of the B.M.A. in the Irish Free State and the Irish Medical Association in a new body representative of the profession in the Free State. He succeeded, in effect, the late Dr. Thomas Hennessy, who for many years was the Irish Medical Secretary of the B.M.A. After five years of most valuable work for his colleagues Dr. Martin relinquished the appointment in 1941 to become the registrar of the Irish Branch of the General Medical Council, which post he occupied until his death. As a physician he made the welfare of his patients his first concern, and his courtesy and kindness as an administrator gained him the affection and respect of all who had dealings with him. An active member of the Royal Medico-Psychological Association, he continued to take an interest in his own branch of medicine long after he had retired from the mental health service: he was chairman of the Irish Division of the R.M.P.A. in 1936–7 and had held the post of Visitor-in-Lunacy to the Chief Justice of the Irish Free State. He was a Fellow of the Royal Academy of Medicine in Ireland.

P. H. MITCHINER, C.B., C.B.E. M.D., M.S., F.R.C.S.

Professor H. A. HARRIS writes: Here in Khartum, at the Kitchener School of Medicine, the news of the death of Philip Mitchiner struck a chill which made one feel his immanence. What a friend he has been to struggling medical schools during their teething troubles in Egypt, Syria, Iraq, the Sudan, the Colonies and Dominions; how prodigal of man-hours devoted to the Royal Colleges, the University of London, the Territorial Association, the O.T.C., and to the country itself in its hour of need. The Sudan Medical Service and the Kitchener School of Medicine, now part of the new University of Khartum, owe much to the young doctors of St. Thomas's Hospital. These doctors know in their marrow how much they owe to Philip Mitchiner. The concentrated ring of pride, kindness, and love in the words I heard a few nights ago under the awe-inspiring starlight of the Nile Valley will stay with me: "I was one of Philip Mitchiner's dressers." His overflowing energy kept him ignorant of the ever-recurring defeats of his stout heart. His spirit could not be defeated, but was ever joyful and triumphant. St. Thomas's Hospital has been a great producer of the foot-sloggers of medicine, both doctors and nurses. Amongst the best and most devoted was Philip Mitchiner, *sans peur et sans reproche*.

J. C. W. writes: May I, as a former house-surgeon of Major-General Mitchiner, add to your obituary notice in the *Journal* of October 25 (p. 943)? Mitchiner's brilliance as a teacher, and his scintillating repartee are, of course, so renowned that they need no further stress from me, but his outstanding attribute was a capacity to inspire loyalty and devotion in his subordinates and patients by intense loyalty to them and by his devotion to their interests. One recalls the time when, knowing that the resident assistant surgeon of the time was in the habit of taking unto himself all emergency surgery, Mitchiner turned out at 2 a.m. for a simple appendicectomy, then sat quietly in the theatre while his house-surgeon performed the operation, and finally turned to the R.A.S., saying, "Will you take pity on an old man, or must I come here every night to see that my house-surgeon gets some experience?" While

I was his house-surgeon, some 17 years after his sojourn in the Balkans, an aged Serb, who spoke nothing but Serbian, came to his out-patient department, after hitch-hiking across a troubled Europe, in order to be operated on by Mitchiner, and I feel that this simple peasant's action speaks louder than any eulogy. "Mitch" has gone, and the world, for many of us, is a vastly poorer place without one who "talked with crowds and kept his virtue, and walked with kings nor lost the common touch."

W. E. GYE, M.D., F.R.C.P., F.R.S.

We are indebted to Dr. H. S. LUCRAFT, of Perth, Western Australia, for the following appreciation of the late Professor W. E. Gye, whose obituary notice appeared in the *Journal* of October 25 (p. 944):

When Professor W. E. Gye retired from the directorship of the Imperial Cancer Research Fund in 1949 he was advised to avoid the English winter by making a journey to Australia (a country of which his wife, Professor Ida Mann, had some knowledge). On first arriving in Australia he was critically ill with bronchopneumonia and congestive cardiac failure, but he eventually made a remarkable recovery. The improvement in his health was followed by an irresistible urge to resume his research work. Fortunately the Western Australian Government quickly saw the opportunity offered to it and so invited him to initiate an experimental laboratory for the public health department. He accepted the invitation, though it involved starting a laboratory from scratch, and threw himself into the work with his usual enthusiasm. A small but good modern laboratory building was made available to him and he commenced forthwith the task of building up a cancer research unit. He imported a stock of 28 inbred mice, now grown to about 1,000, and in collaboration with Professor Mann he resumed the interrupted studies on the time-temperature relationship in the transmission of tumours. Many experiments were begun, and others, sufficient to occupy a research worker for five years, had been planned.

Professor Gye's influence on medicine in Western Australia did not stop short at instituting a cancer research laboratory. Although compelled for health reasons to restrict his physical activities, he nevertheless entered into the medical life of the community. He lectured, in his inimitable style, on the problems of cancer. He investigated, on behalf of the public health department, the claims of several alleged cancer cures. His insistence on a more scientific approach to medicine in general, combined with his own example, will have a lasting influence for good. He had always strongly supported the local demand for the establishment of a medical school in Perth. Owing to his enthusiasm the original cancer research unit which he founded has already grown into a scheme (aided by private subscription and Government subsidy) for a complete medical and research laboratory, or Pathological Research Institute, in Western Australia—an institute which will concern itself not only with cancer research but with research in all branches of medicine. When a medical school does finally arise in Perth the Pathological Research Institute will be attached to it. It is a tragedy that Professor Gye died just as the organization was taking shape and developing into something that will certainly raise the standard of medicine in this part of the world. The work that he began, however, will continue and the institute will serve in years to come as a memorial to him.

Professor Gye's passionate devotion to the search for exact scientific knowledge, his intellectual honesty, and his originality of thought won the admiration and respect of all who came in contact with him. Those who were privileged to know him more intimately, to experience at first hand his kindness, his courage, and the charm of his personality, soon entertained warmer feelings towards him than those of mere admiration and respect. To know Professor Gye was to love him. The medical profession of Western Australia mourns the passing of a great man, and sympathizes deeply with the members of his family in their grievous loss.

Dr. MAYNARD CAMPBELL ANDREWS, who died on November 2 after a long illness, was born on August 16, 1902, and was educated at the University of Cambridge and at University College Hospital, London. He qualified M.R.C.S., L.R.C.P. in 1926, taking the degrees of M.B., B.Chir. two years later and proceeding M.D. in 1932. After qualification he held house appointments at the Royal Alexandra Hospital for Sick Children, Brighton, and at Leicester Royal Infirmary, later becoming casualty officer at the Metropolitan Hospital, London, and clinical assistant at the Samaritan Hospital for Women. He contributed papers to this and other journals on the subject of subarachnoid haemorrhage. In 1931 he settled in general practice at North Wembley, and remained there until his death except for service in the R.N.V.R. throughout the last war. He was honorary medical officer to the Harrow and Wembley hospitals.

J. R. E. and H. W. write: It would surprise many to know that Campbell Andrews was perforce a doctor when he would have been a writer, or that he actually published a novel about his life in some of London's mean streets, a novel marked by promise which was never fulfilled. But, if his aspirations to write were checked, his promise as a doctor was abundantly realized in his life so tragically cut short. He would have been the last to claim that his method of conducting a general practice had anything of special merit in it. Yet, although he was always busy, he was seldom if ever rushed; perceptive of folly or courage, he was tolerant of the one, exalted by the other. He kept abreast of modern medicine; he found time to go on the rounds at a London teaching hospital, not rarely, but as often as he could, and his technique with patients, particularly with sick children, was masterly. He not only had the long purse of patience, he had a Pandora's box of tricks by which 5-year-olds and younger children were beguiled. He loved the fun of student days—was he responsible for the introduction of a live donkey into the rooms of one of his contemporaries whose religiose officiousness needed an abrupt check? Yet with it all he was even as a student very mature. He fell under the spell of Wilfred Trotter, whom he probably appreciated better than his contemporaries, and the artist in him absorbed the wider outlook upon matters other than medicine which Trotter conveyed. It was an outlook tinged with criticism, but he hated hypocrites, would laugh with bores. He was highly critical of the National Health Service Act of 1946, jealous of the old relationship between patient and practitioner which he saw threatened. He was enthusiastic for the Section of General Practice but lately instituted at the Royal Society of Medicine, and, with qualities which would have made him a successful consultant, devoted willingly those gifts to the people of North Wembley, who so appreciated him and who thronged the church at which the funeral service was held. So great was this tribute and so complete this proof, both that he had lived up to his ideals of general practice and that those ideals were right, it was hard to realize that it was only in 1946 that he returned to Wembley from six years in the Navy. Throughout those years he was at sea, in the Far East and the Mediterranean, coming home to England only very occasionally, a record of service which must be unique for a medical officer of his age, but which was characteristic of him. He volunteered for the Special Reserve of the R.N.V.R. just before the war, and his appointment to two of the three ships in which he served (*Ascania*, *Carlisle*, and *Sirius*) was at his own request. He was no firebrand, and sought neither honour nor glory, and as always hated petty discipline, but he believed that as the doctor of an active warship he could be most useful in war. He was completely right: his efficient service saved the lives of many and his personal qualities improved the lives of all. None gained more than did the younger doctors whose good fortune and privilege it was to serve with him, and they alone could guess how much, despite his love of the sea, those years demanded of his physical and moral courage and, above all, how deeply he felt his separation from his wife and two children.

Dr. ALFRED COX writes: It would be a privilege to be allowed to add something to the generous and well-deserved tribute paid to my old friend J. M. MORRIS by Dr. H. R. Frederick (November 15, p. 1104). I made Morris's acquaintance at the historic Swansea Annual Meeting in 1903, but I did not realize the sterling qualities of the man until he took on the secretaryship of the Swansea Division in 1914. He was one of the keenest workers for the Association that I have known and a great encouragement to those of us at Headquarters. He had a puckish sense of humour, which, as Dr. Frederick tells us, was generally transmitted on postcards and in script which few but himself could read—and not always himself. On one occasion I asked him to translate one of his letters which had baffled the B.M.A. staff, and he confessed that some of the words defeated him. It is a good many years since we had met, but Morris will always be remembered by me as a great and lovable "character" and a devoted worker for the Association.

Medical Notes in Parliament

Ex-Service House-surgeons

On November 7 Sir GEOFFREY HUTCHINSON asked Mr. Macleod to consider making special grants to doctors required to give one year's service as house-surgeons on qualification in cases where such doctors had served in Her Majesty's Forces and for that reason were in a higher age group than normally, and in cases where such doctors had family responsibilities. Mr. I. MACLEOD replied that such a house officer might be eligible for a special grant from the Minister of Education, in addition to his salary.

Incidence of Tuberculosis

Replying to Miss I. Ward on November 11, Mr. I. MACLEOD said the percentage of the population suffering from tuberculosis was as follows :

Regional Hospital Area	Number of Notified Cases on Chest Clinic Registers at December 31, 1951	% of Population
1. Newcastle	19,706	0·68
2. Leeds	14,745	0·48
3. Sheffield	25,986	0·63
4. East Anglian	7,449	0·51
5. N.W. Metropolitan	29,616	0·73
6. N.E. Metropolitan	21,750	0·72
7. S.E. Metropolitan	27,601	0·86
8. S.W. Metropolitan	30,471	0·67
9. Oxford	6,474	0·45
10. South-Western	16,839	0·61
11. Wales	21,831	0·84
12. Birmingham	26,013	0·58
13. Manchester	25,297	0·58
14. Liverpool	15,294	0·73

Cost of Hospital Services

Mr. I. MACLEOD on November 11 circulated the following table :

Estimated Hospital Expenditure in 1952–3 per Head of the Population

Regional Hospital Board	Amount per Head
	£ s. d.
Newcastle	4 6 3
Leeds	4 16 0
Sheffield	3 19 0
East Anglian	4 0 8
North-West Metropolitan	5 5 4
North-East Metropolitan	6 0 10
South-East Metropolitan	5 17 5
South-West Metropolitan	6 6 10
Oxford	4 17 10
South-Western	5 10 0
Birmingham	4 5 2
Manchester	4 6 11
Liverpool	5 0 6
Wales	4 14 10

Dentists in Scotland

Commander T. D. GALBRAITH stated on November 11 that in Scotland the number of dentists in general practice taking part in the National Health Service fell from 1,254 at the end of 1951 to 1,210 at the end of October. In the same period the number of dentists in the school service increased from 104 to 131. The present number in this service was equal to the highest number ever before, but was far short of the total that could usefully be employed.

Blind Children

On November 12 Captain E. W. SHORT spoke on the education of blind children. He said the number of prematurely born babies who survived was increasing considerably. In 1949 there were 22,986 premature births and in 1950 24,968, an increase of from 6.1% to 6.4% of total births. Captain Short said blindness was more prevalent among premature babies than among normal babies, and the result was that the incidence of blindness among children was increasing. That was a remarkable result of the Health Service. If, as he feared, the incidence of blindness increased until medical science caught up with it the problem of an increase of accommodation for blind children required to be considered.

Blind babies went to residential homes called Sunshine Homes, run by the National Institute for the Blind, at any age from 5 weeks to 2 years. These homes had a long waiting-list. Side by side with the waiting-list for Sunshine Homes there were vacancies for blind children in primary schools. Either the Sunshine Homes should send their children to primary schools at the age of 5 or more Sunshine Homes should be provided. Inadequate provision was made in point of numbers for blind children who had an additional handicap.

Mr. KENNETH PICKTHORN, Parliamentary Secretary to the Ministry of Education, replied. He said that up to date the blind had, in a sense, got more than their share of special school provision compared with children suffering from other congenital handicaps. Of the 1,300 blind children with which the Ministry of Education was concerned, about 170 were on a waiting-list to go to school. Many parents did not want their children to leave them before they were 5. A considerable number of children on the waiting-list had additional handicaps, and only two Sunshine Homes accepted blind children who had some other defect. He believed that other children on the waiting-list would not have to wait long. The Ministry thought that not more than 200 additional places would be required within the next 10 years. Most of these could be accommodated in existing institutions and in existing buildings. There were children handicapped in other ways than by blindness for whom it was more urgent to provide new buildings or new institutions. The Ministry of Education and the Ministry of Health took pains to see that premature babies who were blind were not neglected. The Medical Research Council was inquiring into the geographical incidence of this condition, which was oddly uneven in distribution for no reasons that were apparent.

The best opinion was that the separation of blind children from partially sighted children in special schools was in the interests of both. Eighteen months ago Warwickshire had opened a school for partially sighted children but had great difficulty in filling it, although all education authorities had been told about it. The Sunshine Home differed from the school where children could go at the age of 5. It was a small school with a high staffing ratio. Seventy-one children, mostly aged under 4, were waiting for places in the homes and had been accepted for them by the National Institute for the Blind. Of these, 29 were subnormal and would have to go to a special kind of Sunshine Home. Of the remaining 42, all aged under 5, 18 would be in Sunshine Homes within the next two or three months. Another 77 children had to be considered for admission to the homes, but of these half were expected to be unsuitable because they suffered from some other kind of handicap.

S.W. Metropolitan Regional Hospital Board

Mr. I. MACLEOD told Dr. R. Bennett on November 13 that, after consulting all the parties concerned and having carefully considered all the views expressed, he had decided that no substantial advantage would be gained by the

creation of a separate region and regional board for the western area of the south-west metropolitan region. The criticisms made by those who wanted a new region could probably be met more economically, and without the loss of the advantages at present deriving from the existence of a single region, by delegation of powers more freely to the western area committee rather than by creating a new region and a new board. He therefore asked the regional board to consider how this wider measure of delegation might be achieved, and had sought its views on a number of suggestions which appeared to be practicable. These suggestions were discussed by representatives of the board and the western area committee with officers of the Ministry. The committee was preparing detailed proposals indicating how it thought the suggestions might be implemented.

Private Patients' Fees

On November 13 Mr. R. S. RUSSELL inquired why patients who used a private ward in a State hospital were not credited with the amount their treatment would have cost if it had been given in a public ward. Mr. I. MACLEOD said the reason was because the statute required that charges for pay-beds must be designed to cover the whole cost of the accommodation and services provided for the patient.

Hospital Staffs

On November 13 Mr. A. BLENKINSOP asked what fresh instructions the Minister of Health had issued limiting hospital medical staffs and proposing reductions in hospital domestic staff. Mr. I. MACLEOD announced that he had opened discussions with the boards of governors about the medical staff establishments of the teaching hospitals.

School Milk.—The Minister of Food stated on November 12 that he was prepared to pay the maximum retail price for tuberculin-tested milk for schools where no alternative supply of safe milk was available.

Attested Cattle.—In Wales 58% of the cattle are attested: in England 30%.

Universities and Colleges

UNIVERSITY OF OXFORD

The Theodore Williams Scholarship in Pathology for 1952 has been awarded to Jeffrey Lima Hayes O'Riordan, Scholar of Pembroke College.

UNIVERSITY OF CAMBRIDGE

Sir Bryan Matthews, professor of physiology in the university, has been appointed a Manager of the Benn W. Levy Fund to December 31, 1955, and Professor J. D. Boyd, professor of anatomy in the university, a Manager of the Charles Slater Fund from January 1, 1953, for four years.

In Congregation on November 8 the degrees of M.B., B.Chir. were conferred on Mrs. Nora Louise Blackwell.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

The following candidates have been awarded the Diploma in Obstetrics: J. F. Adam, Anne Alexander, Maryan G. Anderson, Eileen Atkinson, Margaret A. Austin, Pamela M. Bacon, G. F. Barnes, Edith M. Beecher-Bryant, J. D. Belt, J. S. G. Blair, W. W. Bowie, J. D. Brackenridge, Gladys V. Bradshaw, J. M. Brown, Janet C. Bryce, A. E. R. Buckle, M. G. Budden, D. W. Bull, Sheila G. Burnie, A. F. Bushby, Mary Campbell-Mackie, I. T. Carrie, C. Cassar, D. J. Cawthorne, J. S. W. Chambers, Vera Choithramani, Sheila R. Clarke, P. W. Clements, June P. Cooper, K. V. Cooper, J. H. Cowie, Ann C. Coyle, O. J. Curl, J. W. B. Dalgleish, J. K. Davidson, H. F. Davies, Elizabeth Dennys, J. C. Dilley, P. R. Dixit, F. B. Dobbs, D. J. Dobson, Margaret K. Douglas, Diana F. J. Duncan, W. A. W. Dutton, G. F. E. Edmondson-Jones, Mary G. Eldridge, W. Ellenbogen, J. McG. Elliott, Luba Epsztejn, J. Eyton-Jones, Margaret D. Findlay, G. R. C. Fisher, Mary L. Fraser, G. C. Galea, Barbara E. Gibbs, A. Gillespie, D. L. Golightly, J. Ll. Goodger, Anne L. M. Graham, D. A. H. Grieve, S. Hacking, A. B. Haigh, Ethna J. Halpin, I. A. El-W. Hamdy, Marion Hanson, H. A. Harding, Elizabeth M. Harpur, D. T. G. Harris, Helen J. Harthoorn, R. Hewitt, J. M. Hiddleston, Margaret I. Hill, J. A. Holmes, J. L. Honig, J. M. Hood, R. A. St. C. Hoyte, Anne L. Hunter, Anne E. Jameson, M. H. Jameson, Helen Jessler, J. M. Jewitt, G. A. H. Jones, W. T. Joseph, Margaret Kassab, J. A. N. Keane, G. E. Kelly, Sybil V. Kinley, Frances E. W. Kinnaird, Frances E. Kirk, A. L. Kirkland, Chung Yue Lai, E. C. Lewis, Isabel J. Lim, M. D. W. Low, Helen M. M. McCallum, J. M. S. McCoy, Yvette McCoy, J. A. McCraith, Sarah C. McEwan, Anne M. McKechnie, J. G. McKenny, Edith M. McLean, Margaret E. Maclean, B. N. McQuade, D. H. McVie, A. R. Magarey, Maureen A. F. Malcolm, M. D. Manion, J. G. Markus, G. F. G. Marshall, G. G. M. Miles, J. L. Miller, R. C. Molk, Elisabeth Monkhouse, D. J. R. Morgan, June Morgan, K. D. Mullen, B. J. Murphy, S. Muscat, J. P. Norris, K. R. Norton, K. F. O'Callaghan, D. W. Orton, T. G. Osmond, R. B. Ottley, H. J. G. Palmer, R. T. Parr, P. Paul, F. S. Perry, R. J. Pett, Mary P. Phelan, K. B. Pillai, S. J. S. Polwin, Joan M. Ponsford, F. J. Powell, R. B. Prowse, Hilary R. Pullon, D. W. Quantrill, D. J. H. Rogers, A. Sabhesan, P. Sarin, Rachel D. R. Sasieni, M. K. Sawday, G. C. W. Sharpe, R. W. Simpson, S. L. Skoll, H. Stabile, A. J. H. Stephens, J. E. L. Sutcliffe, C. G. W. Sykes, P. K. Sylvester, D. Tacchi, A. D. El-Tannir, A. R. Taylor, J. Taylor, J. G. A. Troup, P. W. Tucker, J. B. Turtle, I. S. Waller, Daphne M. L. Walters, Paula M. Watkin, Joyce M. Watson, W. L. Whitehouse, Kathleen M. Witham, L. M. Wolf, Elizabeth J. A. Yool.

Vital Statistics

Week Ending November 8

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,976, whooping-cough 1,449, diphtheria 27, measles 11,264, acute poliomyelitis 117, dysentery 213, paratyphoid fever 2, and typhoid fever 4.

Infectious Diseases

The chief feature of the returns of infectious diseases during the week ending November 1 in England and Wales was an increase of 2,045 in the number of notifications of measles from 9,178 to 11,223. Other rises in incidence were 177 for dysentery (from 236 to 413), 243 for whooping-cough (from 1,206 to 1,449), and 100 for scarlet fever (from 1,994 to 2,094).

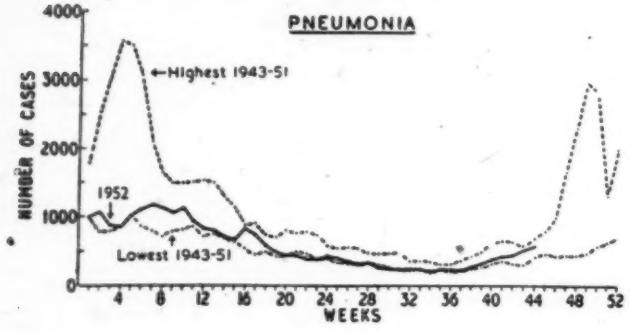
Only once in the past 13 years (in 1940) has the incidence of measles been so high at this period of the year. The largest increases during the week were 265 in Essex, from 677 to 942; 260 in Yorkshire West Riding, from 845 to 1,105; 158 in London, from 1,094 to 1,252; 128 in Durham, from 397 to 525; and 118 in Middlesex, from 509 to 627. The only large fluctuation in the trends of whooping-cough was a rise of 51 in Yorkshire West Riding, from 139 to 190. Despite the increasing trend of scarlet fever, the largest variation in the returns was a fall of 80 in London, from 200 to 120. The number of notifications of diphtheria, 29, was one more than in the preceding week. The chief features of the returns for diphtheria were a decrease of 5, from 9 to 4, in Lancashire, and an outbreak involving 5 persons in Staffordshire, Coseley U.D.

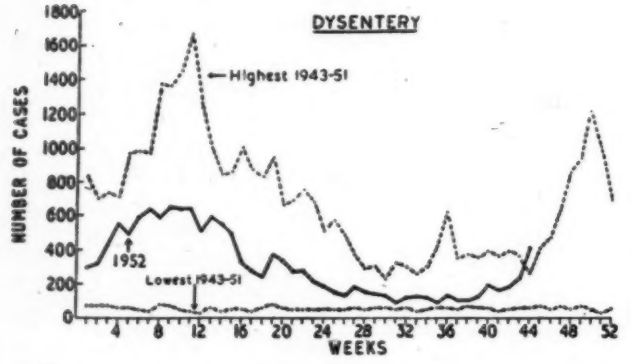
The number of notifications of acute poliomyelitis, 86, was 10 less for paralytic and 5 less for non-paralytic cases than in the preceding week. The notifications are slightly more numerous in the southern section of the country than in the north. The largest returns were Surrey 9, Kent 9, Middlesex 9, and Essex 8.

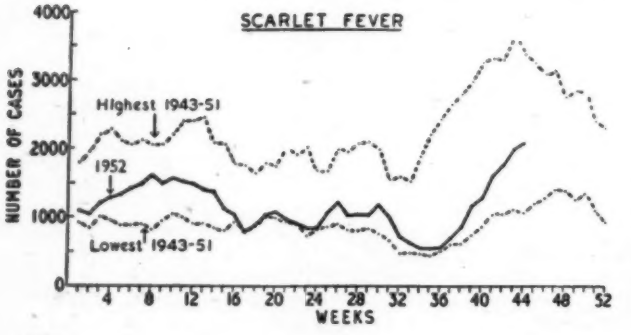
The rise in the incidence of dysentery was due to an increase of 136 in Lancashire, from 121 to 257. The largest returns in this county were Blackpool C.B. 202, Liverpool C.B. 16, and Blackburn R.D. 15. In the preceding week 94 cases were notified from Blackpool C.B. in an outbreak which concerned four day-schools. The largest of the other returns in the country were London 18, Kent 16 (Margate M.B. 14), Middlesex 13, Yorkshire North Riding 11 (Middlesbrough C.B. 11).

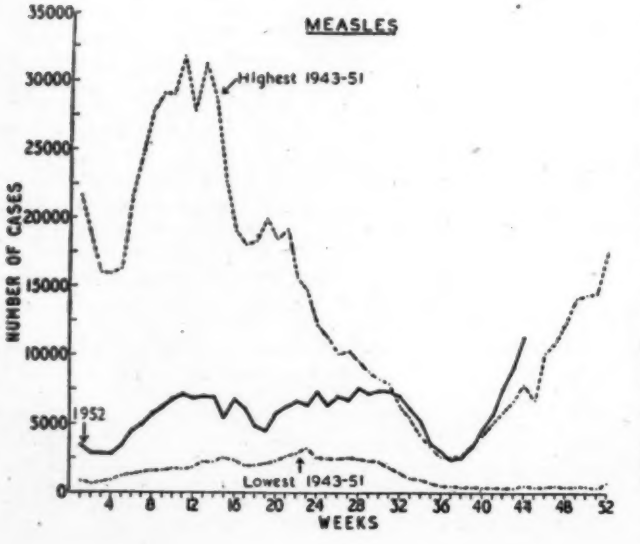
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1943–51 are shown thus - - - - - - -, the figures for 1952 thus ————. Except for the curves showing notifications in 1952, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending November 1 (No. 44) and corresponding week 1951.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1952					1951				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	29	3	12	1		46	5	8	1	1
Dysentery	413	18	95	0		175	34	64	0	1
Encephalitis, acute	2	1		0		4	0	0	0	
Enteric fever:										
Typhoid	8	1	0	1		2	0	0	0	1
Paratyphoid	7	2	1 (B)	0		26	0	0	0	
Food-poisoning	85	7		0		122	11		3	
Infective enteritis or diarrhoea under 2 years				11	22				24	35
Measles*	11,223	1252	154	51	63	1,993	65	85	169	172
Meningococcal infection	34	3	19	4	1	33	2	10	1	1
Ophthalmia neonatorum	38	3	10	0		57	1	9	0	
Pneumonia†	575	48	292	1	1	510	49	161	2	
Poliomyelitis, acute:										
Paralytic	65	3	6	2	6	62	3	18	0	7
Non-paralytic	21	1				20	2			
Puerperal fever§	259	43	10	2	1	242	30	11	1	1
Scarlet fever	2,094	120	345	27	84	1,067	117	296	30	44
Tuberculosis:										
Respiratory			160	25				139	31	
Non-respiratory			20	4				26	3	
Whooping-cough	1,449	77	83	32	84	1,477	51	301	65	68

DEATHS in Great Towns	1952					1951				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0		0	0	*0*	0	*0*	0	0
Dysentery	1	1		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0		0		*0*	0	*0*	0	
Infective enteritis or diarrhoea under 2 years	6	1	2	0	0	*11*		*2*	1	0
Influenza	11	0		0	0	*17*	3	*3*	0	1
Measles		1		0	0		0	*0*	0	0
Meningococcal infection		0					0	*0*		
Pneumonia	200	25			5	*243*	42		8	6
Poliomyelitis, acute	1	0			0	*4*	0			0
Scarlet fever		0		0	1		0	*0*	0	0
Tuberculosis:										
Respiratory	94	8	8	3	9	*155*	23	*17*	4	8
Non-respiratory		2	5	0	0		3	*4*	1	1
Whooping-cough	1	0		0	0	*1*	0	*1*	0	0
Deaths 0–1 year	211	19	37	7	8	*236*	25	*38*	9	6
Deaths (excluding stillbirths)	5,027	714	588	87	140	*5,180*	850	*549*	99	131
LIVE BIRTHS	7,212	1099	865	175	355	*6,284*	1052	*749*	173	386
STILLBIRTHS	182	22	19			*168*	24	*29*		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Second Volume of "Any Questions?"—The new volume of "Any Questions?" comes out this week. It is packed with useful information selected from our weekly page of doctors' queries. Great care has been taken to see that the new volume complements its predecessor without overlap: for instance, such subjects as "marital problems" and "immunization," which were only lightly touched upon in the first volume, are extensively dealt with in the second. It is still necessary to limit the number of copies printed, so an early order to the Publishing Manager (B.M.A. House, Tavistock Square, W.C.1) is strongly advised. Ten thousand copies of the first volume were printed, and now only a very few are left. The cost of each volume is 7s. 6d. (postage 6d. extra). In the second volume 198 questions from doctors are answered by our experts.

Weights and Measures.—Although most scientists and many doctors hanker for the replacement of the Imperial system of weights and measures by the more logical metric system, there is little likelihood of this happening in Britain for many years. Last week in Parliament the President of the Board of Trade, Mr. Peter Thorneycroft, said that the Government was not prepared to make the change. He was being questioned about the report of the Weights and Measures Committee, published as long ago as May, 1951 (see *British Medical Journal*, 1951, **1**, 1195), in which a gradual change from Imperial to metric system had been recommended. Mr. Thorneycroft added that consultation with the United States and Commonwealth Governments had shown widespread support for a legal definition of the relationship between the Imperial pound and yard and the metric kilogram and metre. There is to be further consultation, however, before any legislation is introduced.

Metropolitan E.N.T. Hospital.—The Minister of Health has asked the South-west Metropolitan Regional Hospital Board to postpone moving the Metropolitan E.N.T. Hospital to the Western Hospital, Fulham, pending discussions between his officers and the board. In a letter sent to the board on November 14 it was stated: "As there are certain aspects of the move which the Minister would like to consider further—particularly as regards the dangers of infection at the Western Hospital—he would be glad if the board would postpone the impending move for the time being." On November 18 a meeting between the representatives of the board and the Ministry was held to discuss the matter.

Royal Society's Royal Medals.—Of the two royal medals awarded this year, with the approval of the Queen, one goes to Sir Frederic Bartlett, until very recently professor of experimental psychology at Cambridge, and honorary director of the Medical Research Council's applied psychology research unit. The award is for the creation of an experimental school of psychology "which has established under his leadership an outstanding position recognized internationally as without superior."

What is Race?—When bitter racial conflicts are disturbing more than one continent, it is refreshing to meet a simple, cool, amusing, and informative appraisal of the nature of race. On sale at H.M. Stationery Office (price 5s.) is an illustrated Unesco booklet called "What is Race?" It sets itself to answer scientifically three questions: "Is there a pure race?"; "Is there a superior race?"; and "Are there absolute and unchangeable race differences?" It succeeds admirably, and in a way which will appeal to both savant and schoolboy.

Education and Treatment of Spastics.—The National Spastics Society, composed almost entirely of the parents of spastic children, with Professor J. M. Mackintosh as president, has recently launched an appeal for a million pounds. According to the Society's estimates, stated to be conservative, there are in Britain about 10,000 spastic children (compared with 3,000 blind children), and a further 20,000 spastic adults. The present provision of special schools for spastics is said to suffice for less than 1,000 of these children, and the Society's main object in launching its appeal is to establish more centres for their treatment and education. The address of the Society is 20, Pembroke Road, London, W.8.

The Common Cold.—The common cold research unit at Harvard Hospital, Salisbury, is appealing for 600 volunteers next year to screen experimental materials for the presence of cold virus. The unit is now trying to grow the virus in human tissue cultures, as other methods, such as the use of fertile hen's eggs and guinea-pig inoculation, have proved ineffectual. So far nearly 3,000 volunteers have assisted the unit.

International Biological Standards.—Three new international standards were established at last month's meeting of World Health Organization experts, and two others were replaced by fresh standards. The new ones were for dimercaprol (B.A.L.), scarlet fever streptococcal antitoxin, and anti-*Brucella abortus* serum; the replacements were for insulin (the third) and penicillin (the second). International standards for sera are kept at the State Serum Institute, Copenhagen, and all other international standards at the National Institute for Medical Research, Mill Hill.

Florey Trust.—A recent example of the generous interest taken by industry in research at the universities is the endowment at Lady Margaret Hall, Oxford, of a medical research fellowship by four firms: Boots Pure Drug Company, the Distillers Company, Glaxo Laboratories, and Imperial Chemical Industries. The benefaction, to be known as the "Florey Trust," is in commemoration of the discovery of the chemotherapeutic action of penicillin and its introduction into medicine through the work done at Oxford by Sir Howard Florey and the team of scientists working with him. The first holder of the fellowship will be Dr. Margaret A. Jennings. She was a member of Florey's original team, and has been a research member of the School of Pathology at Oxford since 1936.

Conference on Kwashiorkor.—Although only a few years ago kwashiorkor had hardly been heard of outside the areas where it is endemic, its importance as a threat to child health in the Tropics, especially in Africa, is now widely appreciated. At a conference on malnutrition in African mothers and children which opened at Fajara in the Gambia on November 19, kwashiorkor was the main subject of discussion. Attending the conference, which is under the auspices of the Commission for Technical Co-operation in Africa South of the Sahara (C.C.T.A.), are delegates from the Governments of Belgium, France, Portugal, Southern Rhodesia, the Union of South Africa, the United Kingdom (Professor B. S. Platt and Professor A. A. Moncrieff), and African territories. In addition there are observers from F.A.O., W.H.O., and other interested bodies. Fajara is the village where the field research station of the Medical Research Council's human nutrition research unit is situated. Professor Platt is the unit's director.

Freud's Archives.—Plans have been made by Dr. Bertram D. Lewin, of New York, and others to collect letters to and from Freud, his original manuscripts, photographs, and other material about him which are at present dispersed. The Sigmund Freud Archives, as the collection is to be called, will be housed by the Library of Congress, Washington, D.C. Not all the documents will be immediately available to students, as both the donors and the organizers of the archives may insist on selected documents being kept confidential for many years. The headquarters of the archives is at 575, Madison Avenue, New York.

Adventure for Doctors.—The British Schools Exploring Society invites applications for the posts of honorary physician and honorary surgeon to its 1953 expedition to British Columbia (July 28 to September 24). The cost to each member of the expedition will be about £150. Appli-

cants should write to the society's secretary, c/o Royal Empire Society, Northumberland Avenue, London, W.C.2.

Liddle Triennial Prize.—The subject for the 1955 Liddle Prize essay has now been announced: it is "The Effect of Hormones on the Reaction of the Tissues to Injury." The prize is valued at £120. Further details may be obtained from the Dean of the London Hospital Medical College, Turner Street, London, E.1.

Emergency Bed Service: Applications and Admissions.—During the seven days ending November 17 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 1,069, of whom 91.20% were admitted.

Bequests.—Professor George Grey Turner left his collection of Hunterian Letters to the Royal College of Surgeons of England and £500 to be applied to the preparation and publication of a further volume or volumes of Plarr's *Lives of the Fellows*. In addition he left £500 to the School of Medicine in King's College, Newcastle-upon-Tyne, to form a Grey Turner Fund, the interest to provide an honorarium for a lecture on some aspect of the history of surgery.

Sir Neil Hamilton Fairley, consultant in tropical diseases to the Army, and noted for his wartime researches on malaria, is in Australia. He arrived from Malaya, where he had been investigating reports of the emergence of proguanil-resistant strains of malaria. Earlier in the year, in East Africa, he conducted trials in human volunteers to see if proguanil would protect them against resistant strains of malarial parasites.

Dr. E. Taylor Cummings has been re-elected Mayor of Freetown, Sierra Leone, for the fifth time in succession.

Royal College of Physicians.—The Duke of Edinburgh was welcomed by Sir Russell Brain as a Fellow of the Royal College of Physicians when he dined at the College on November 18.

COMING EVENTS

Fourth Ciba Foundation Lectureship.—Dr. G. W. Corner, of the Carnegie Institution of Washington, Baltimore, will give the Fourth Ciba Foundation Lecture on behalf of himself and Dr. A. Csapo on December 4, at 5 p.m. at the Royal Society of Tropical Medicine and Hygiene, London, W.1. The subject of the lecture is "The Action of Ovarian Hormones on Uterine Muscle," and Sir Henry Dale, O.M., will be in the chair. Those wanting to attend the lecture should apply for tickets of admission to the Assistant Secretary, Ciba Foundation, 41, Portland Place, London, W.1.

The Victor Horsley Memorial Lecture, on "Ischaemia in Surgery," will be delivered by Sir James Learmonth in the Old Library, B.M.A. House, Tavistock Square, London, W.C.1, on December 11 at 5 p.m.

SOCIETIES AND LECTURES

Details in this column are necessarily brief. Further information and tickets where required (marked ●) should be obtained from the institution concerned.

Monday, November 24

●INSTITUTE OF CHILD HEALTH.—5.30 p.m., Professor W. I. B. Beveridge: Resistance and Susceptibility to Viruses.
INSTITUTE OF PSYCHIATRY.—4.30 p.m., Dr. E. Stengel: lecture-demonstration.
MANCHESTER MEDICAL SOCIETY.—(1) At Dental Hospital, 5 p.m., Professor V. F. Lambert: Tumours of the Palate; (2) At Manchester University, 9 p.m., film, followed by discussion: Carcinoma of the Cervix.
MEDICAL SOCIETY OF LONDON.—8.30 p.m., discussion on bronchitis.
ROYAL EYE HOSPITAL.—5.30 p.m., Professor T. Nicol: Applied Anatomy of the Orbit.

Tuesday, November 25

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor Adrien Albert, D.Sc. (Australian National University): Selective Toxicity.
CHADWICK TRUST.—At 90, Buckingham Palace Road, S.W., 2.30 p.m., Mr. J. Rawlinson, M.Eng., M.I.C.E.: History of the Main Drainage of London.
●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Professor H. Barcroft: Peripheral Circulation.
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 4.30 p.m., Sir Stanford Cade: Surgery after Pelvic Irradiation.
PADDINGTON MEDICAL SOCIETY.—At St. Mary's Hospital, 8.45 p.m., discussion: The Recommendations of the Working Party.
WEST END HOSPITAL FOR NERVOUS DISEASES.—5.30 p.m., Dr. Douglas Gordon: Radiological Methods in Neurology.

Wednesday, November 26

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Benign Epithelial Tumours.
●LONDON MARRIAGE GUIDANCE COUNCIL, 78, Duke Street, Grosvenor Square, W.—6.30 p.m., Dr. Mary Barton and Dr. Ethel Dukes: Psychological and Medical Aspects of A.I.D.
NORTH-WESTERN TUBERCULOSIS SOCIETY.—At Aintree Hospital, Liverpool, 5.30 p.m., Dr. H. Noel Bleasdale: Sanatorium Nursing—Care and Rehabilitation of the Ex-patient Nurse.
ROYAL EYE HOSPITAL.—5.30 p.m., symposium on methonium.
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Weild Lecture, by Mr. T. Holmes Sellors: Cancer of the Lung.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. A. Austin Eagger: Health in the Factory—The Slough Industrial Health Service.

Thursday, November 27

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor Adrien Albert, D.Sc. (Australian National University): Selective Toxicity.
HONYMAN GILLESPIE LECTURE.—At University New Buildings, Edinburgh, 5 p.m., Dr. J. A. Fraser Roberts: Inheritance of Sex-linked Abnormalities in Man
INSTITUTE OF PSYCHIATRY.—3 p.m., Professor J. Elkes: Pharmacological Method in Psychiatric Research.
LIVERPOOL MEDICAL INSTITUTION.—8 p.m., Dr. Robert Hughes: Treatment of Coronary Thrombosis with Anticoagulants; Mr. B. J. Bickford: Treatment of Angina Pectoris by Sympathectomy.
MANCHESTER MEDICAL SOCIETY.—8 p.m., Dr. A. H. Galley: Kidney in Relation to Anaesthesia and Analgesia.
OXFORD UNIVERSITY.—At Nuffield Orthopaedic Centre, Wingfield-Morris Orthopaedic Hospital, 8.30 p.m., Mr. R. G. Pulvertaft: The Injured Hand and its Repair.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Major-General Sir Heneage Ogilvie: A Eulogy of the Yes-man.
ROYAL EYE HOSPITAL.—5.30 p.m., Miss M. Savory: Some Newer Therapeutic Measures.
ST. ANDREWS UNIVERSITY.—At Materia Medica Department, Dundee, 5 p.m., Professor G. A. G. Mitchell: Innervation of the Thoracic Viscera.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. D. Curran: lecture-demonstration in psychiatry.
WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At West London Hospital, 2.30 p.m., clinical afternoon.

Friday, November 28

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr P. F. Borrie: Vascular Disorders.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—4.30 p.m., Mr. A. R. Dingley: The Use of Sulphonamides in Otitis Media.
MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.—7.30 p.m., Dr A. N. Ashworth: Cortisone in the Treatment of Syphilis of the Eye.
ROYAL EYE HOSPITAL.—4.30 p.m., Mr. A. J. Cameron: Medical Ophthalmology
ROYAL MEDICAL SOCIETY, Edinburgh.—8 p.m., address by Mr. P. W. Brand.

Saturday, November 29

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 11 a.m., Dr. C. L. Cope: Anaemia and Pregnancy; 12 noon, Dr. Mary Barber: Outbreak of Sepsis in a Maternity Ward.

APPOINTMENTS

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—*Senior Registrar in Chest Medicine at East Norfolk Chest Clinic*, R. W. Pettigrew, M.B., Ch.B. *Medical Registrar at Foxhall Hospital, Ipswich*, N. O. Ascroft, M.B., Ch.B. *Medical Registrar at Papworth Hospital*, Mary T. Keyes, M.B., Ch.B.
MAYER, HELEN M., M.R.C.S., L.R.C.P., M.R.C.O.G., Part-time Obstetrician and Gynaecologist (Consultant), The Mothers' Hospital (Salvation Army), Clapton, London, E., North-East Metropolitan Regional Hospital Board.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Hamilton.—On October 28, 1952, at Harbour Breton Cottage Hospital, to Rosemary (formerly Haydock), M.B., B.S., wife of Thomas R. Hamilton, M.B., B.S., of Hermitage, Newfoundland, Canada, a son.
Mathieson.—On October 9, 1952, at 24, Richmond Road, Middelburg, Cape, South Africa, to Sylvia (formerly Lidbetter), wife of Dr. Ian Mathieson, a son.

MARRIAGES

Mullins—Rowdon.—On September 20, 1952, at Johannesburg, South Africa, David Francis Mullins, B.M., B.Ch., to Mary Evangeline Hooker Rowdon.

DEATHS

Andrews.—On November 2, 1952, Maynard Campbell Andrews, M.D., of North Wembley, Middlesex, aged 50.
Berkowitz.—On October 25, 1952, at Srinagar, Kashmir, India, Harold Guenther Berkowitz, M.D., formerly of Oxford.
Gibson.—On November 4, 1952, George Gibson, L.R.C.P.&S.Ed., L.R.F.P.S.Glas., Surgeon Captain, R.N., retired.
McKelvie.—On November 3, 1952, John Douglas McKelvie, M.D., of Blofield, Norwich.
Owen.—On October 30, 1952, William Griffith Owen, M.R.C.S., L.R.C.P., of "Hendre," Penygroes, Caern.
Turner.—On November 4, 1952, at his home, "Ravensnest," Hythe, Southampton, Hants, Arthur John Turner, M.B., B.S.
White.—On November 3, at his home, 172, Monument Road, Edgbaston, Birmingham, James Atkin Henton White, M.D., F.R.C.S.Ed., aged 81.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Routine Health Examinations

Q.—*Popular books on health frequently advise their readers to see their doctors periodically for a "check-up." What routine examinations are advised in the case of young children, young and middle-aged adults, and old people? It is presumed that there is no complaint of ill-health. Should such examinations include radiography of the chest and a blood count?*

A.—The aims of periodic examination include the early detection of remediable defects, getting to know persons for the supervision of whose health responsibility has been accepted, education in habits of personal hygiene, and the collection of information to define what is normally to be expected. The wording of the question concentrates on the first of these aims, and it excludes the large proportion of persons who use the advice given in popular books on health as their excuse for an interview about some more pressing personal problem.

In routine arrangements due allowance must be made for particular occupational risks, geographical locality, the type of population to be examined, and local facilities, such as, for example, miniature radiography at the practitioner's disposal. In Britain, the routine test most commonly advised is chest radiography, if possible annually from the age of 15 to 25 and thereafter less frequently, but also at special times—for example, on entering new employment, with the object of protecting fellow workers from sources of tuberculous infection. Chest radiography is not advised routinely for young children, or for old people, in the certain absence of symptoms. In fact, no other special tests, with the possible exception of haemoglobin estimation in women over 20, are advised for "blind" routine use.

Periodic preventive or health examinations, like other clinical examinations, depend on a good clinical history, physical examination, and the particular circumstances. In young children, knowledge of the child and its progress are the main purpose, and probably the smaller the amount of physical examination consistent with this aim the better. Defects steadily accumulate with years, until in old persons they are usually numerous. In spite of this, old persons outside selected or hospital groups usually complain less, and carry on as long as they feel useful. To help them to do this, routine attention to painful foot troubles and other factors limiting their power to get about, and to incontinence—more particularly stress incontinence of urine in women—and the provision of hearing-aids or glasses, where necessary, are most often rewarding. Inquiry into family circumstances may show the need for temporary relief to the younger generation from an otherwise unremitting burden of caring for old people.

Arrest of Myopia

Q.—*Will any treatment, medicinal or by correction of refractive errors, arrest the progress of myopia in a child?*

A.—All authorities are not agreed on the effect of treatment of refractive errors by spectacles as a means of arresting the progress of myopia in a child. The most authoritative opinion at the present time is to consider the average case of myopia as genetically determined and therefore in the main not amenable to such treatment. So far as the actual progress of the myopia is concerned, it is obvious that the refractive error should be corrected if for nothing else than to facilitate the mental development of the child, and the elimination of eyestrain by spectacles can, of course, do nothing but good. The question of medicinal treatment depends entirely on the case; if the child is healthy and well the indications are that medicinal treatment is not of value. If, however, as often occurs, the onset or the rapid progress of the myopia is associated with debility or illness, the treatment of such a condition should receive every attention. In recent times calcium has been suggested as an appropriate medicinal remedy, but the scientific evidence in favour of this is meagre and it is probably of little value, except perhaps in such cases where a definite deficiency of calcium can be shown to exist.

Temperature and the Leucocyte Count

Q.—*Does a high external temperature or fever cause any variation in the leucocyte count?*

A.—Artificial fever (hypertherm) causes a polymorph leucocytosis with a shift to the left of the polynuclear count. Residence in a hot climate—for example, in Iraq or Egypt—causes a shift to the left in the polynuclear count which disappears on return to England. The reason for these changes is obscure. Significant changes in the monocyte and lymphocyte count with external heat or with artificial fever have not been reported, although sunlight and ultra-violet light may increase both lymphocytes and polymorphs slightly. Excellent reviews of physiological variations in the leucocyte count are given by Garry and Bryan[1] and Sturgis and Bethell.[2]

REFERENCES

1 *Physiol. Rev.*, 1935, **5**, 597.
2 Ibid., 1943, **23**, 279.

Kidney Transplants

Q.—*What are the chances of successful transplantation of the kidney in humans? Is it likely to become a practical treatment for those with serious kidney disease?*

A.—The chances must be regarded as negligible. Recent American claims for the successful transplantation of kidneys between dogs have not been substantiated, and the best evidence is that kidneys so grafted are destroyed (as a consequence of immunological incompatibility) far too soon for them to be of any practical use. The human being is not likely to be less exacting or "individualistic" than the dog. Kidney transplantation is not likely to be practicable until some solution has been reached of the general problem of making tissues from one human being grow in the body of another.

Colon Spasm

Q.—*What findings are necessary to establish a diagnosis of colon spasm? What is the prognosis? Are any special complications, such as intestinal obstruction, for instance, liable to occur?*

A.—The term "colon spasm" has come to be used rather loosely. Spasmodic contractions of the colon will obviously occur as secondary manifestations of various diseases—for example, organic obstruction from neoplasm, acute inflammations such as ulcerative colitis and dysentery, and even chronic appendicitis. The entity colon spasm undoubtedly exists, but it is very rare: it is a sudden cramp-like contraction of the colon (usually the sigmoid) which, with its symptoms of sudden pain, nausea, absolute constipation, and some distension, is almost invariably diagnosed as acute obstruction and operated on as such. In a genuine case—the patients usually being women and of a highly strung temperament—the affected colon will be found to be firm, contracted, and pale. Often, however, nothing will be discovered, the anaesthetic having produced relaxation of the spasm. If a non-operative diagnosis can be made, atropine and narcotics will produce rapid relief of symptoms.

"Asthma of the Bowels"

Q.—*Is there any relationship between asthma and attacks of mucous colitis? Could colitis (frequent attacks of diarrhoea with some pain and mucus but no blood) be related to treatment of the asthma with ephedrine and adrenaline? What treatment is advised for the bowel symptoms?*

A.—In the older literature mucous colitis has been referred to as "asthma of the bowels," and there are very occasional references to the relation of these two conditions. This is not altogether surprising, for mucous colitis, which is generally accepted as a neurosis, may very occasionally be due to an allergic reaction to a food, while asthma, which is generally accepted as dominantly an allergic condition, often has a psychological factor in its aetiology.

It is very unlikely that the colitis is related to the treatment with ephedrine and adrenaline, but this could be investigated by their exclusion from treatment for a few weeks. The bowel-symptoms might be investigated on the lines suggested above, and treatment applied to the underlying condition rather than to the bowel symptoms themselves.

Shortest Interval Between Two Confinements

Q.—*Do studies of primitive communities throw any light on how short an interval can exist between two confinements in the same mother, it being assumed that the second confinement is at full-term and is not a multiple birth?*

A.—The writer does not know of any report or studies carried out amongst primitive communities which deal with this problem. Moreover, since lactation tends to delay ovulation after pregnancy and since artificial feeding of the newborn is most common in civilized communities, extreme frequency of child-bearing is more likely to be seen in the latter. Probably the best evidence on how soon conception can occur after a confinement is provided by studies on the times of the first ovulation and menstruation after delivery. The results of these indicate that even if lactation is suppressed the first ovulation rarely if ever occurs before four to six weeks after delivery, and may be later. If the woman is breast-feeding it is nearly always later. The first menstrual periods are often anovular. This means that the shortest possible interval between two confinements at term is about 44 weeks. Examples of a 50-week interval are not uncommon in this country. After abortion ovulation may be as early as two weeks.

If the inquirer is looking for "the record" shortest interval between two deliveries, then difficulty will be encountered. The reasons for the difficulty are the wide but normal variations in the duration of pregnancy; the normal variations in the birth weights of babies, which may make it impossible to say if the second labour is premature; and, in extreme cases, the possibilities of superfoetation and superfecundation.

Garrulitas Vulvae

Q.—*What treatment is advised for a young multipara whose vagina fills with air when she bends down and then empties itself with an embarrassingly audible squelch when she stands up again? In the left lateral position the vaginal walls are not in apposition, and the cervix is clearly visible on simply separating the labia. There is no prolapse.*

A.—This phenomenon is rarely mentioned in modern textbooks, but is described in many of the gynaecological works of the last century. It is most often called "vaginal flatus," but is delightfully referred to by one old writer as "garrulitas vulvae." It is caused by a deficient perineum and atonicity of the muscles around the lower vagina. This allows the introitus to gape so that air enters the vagina in certain postures—more particularly if the woman bends low or kneels down, as in scrubbing the floor. Exercises to strengthen the pelvic-floor muscles might help a good deal in this case, but, failing that, perineorrhaphy will be necessary to effect a cure.

Treatment of Yaws

Q.—*What advantages has the treatment of yaws with penicillin over arsenotherapy?*

A.—In adults two injections of 1.2 mega units procaine penicillin G in oil with 2% aluminium monostearate, given at an interval of 3–5 days, are followed by results as good as, and possibly better than, those following six injections of neoarsphenamine. Treatment with penicillin is followed by fewer toxic reactions than after arsenic, it is technically easier to administer (being given intramuscularly instead of intravenously), and it is slightly cheaper. The small number of injections required is of particular advantage in treating indigenous peoples in the Tropics, many of whom default after two or three injections have been given.

NOTES AND COMMENTS

Angular Stomatitis.—Dr. H. C. COOPER (London, S.W.7) writes: Regarding the expert's reply to the question on angular stomatitis (November 1, p. 1006), if the patient uses lipstick I would suggest that she should cease doing so and see the result after one month.

Dr. J. HEGINBOTHAM (near Stockport) writes: I have found that some cases of this condition are associated with achlorhydria, and that even though the blood picture is normal the cracks clear quickly with an injection of vitamin B_{12}. They tend to relapse when the B_{12} is stopped. Sometimes a compound B vitamin appears to help. I have wondered whether it is a pre-pernicious-anaemic state.

Dr. H. R. VICKERS (Sheffield) writes: Since I described the association between angular stomatitis and sensitivity to denture materials in the *British Medical Journal* (1949, **2**, 1091) I have seen many of these cases, and in every one in which the cause was due to sensitization of the denture material the gums underlying the dentures were red and inflamed. This is as would be expected, since when a denture is being worn it is in effect carrying out a patch test. I would like to know on what evidence the author of your answer is able to state that "an allergic sensitiveness to the material of the dentures may determine an angular stomatitis without necessarily producing inflammation inside the mouth." If the buccal mucous membrane underlying the denture is not reddened and if the patch test to the denture applied to some other area of the skin is negative, it is difficult to see how the causes can be attributed to an "allergic sensitiveness. . . ." It may be that the patch test is negative and the underlying mucous membrane not affected, and the angular stomatitis clears up when the dentures are not worn. In this case the cure may be due to removal of causes other than "allergic sensitiveness"; it is more likely to be due to removal of some mechanical factor associated with dentures. One such cause not mentioned is seen in patients having a rather small mouth: these patients often have difficulty in inserting and removing large dentures, thereby producing traumatic lesions of the oral commissures.

OUR EXPERT writes: My reply was not, of course, intended to be entirely comprehensive. I would agree that lipstick may cause an angular stomatitis, though the red margin of the lip is usually involved as well. I would accept that some patients with unexplained angular stomatitis may respond to B_{12}, but have little experience of this. While agreeing with Dr. Vickers's thesis in general, the writer has seen a positive skin patch test from dentures where angular stomatitis has not been associated with any affection of the mucosa. This is not surprising, since we are familiar with allergic reactions of mucosa without epidermal response and the reverse, as from pollens, *Primula obconica*, and dusts. I agree that with sensitization to dentures it is usual, however, to have involvement of the mucosa, but in his article Dr. Vickers quotes Rattner as describing stomatitis from plastic dentures where a patch test on the skin had been negative and that on the mucosa positive.

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